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SPASTIC PARALYSIS.3

By RAYMOND GREEN, M.B. (Sydney),
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Patients suffering from spastic paralysis, when seen by the pædiatrician most commonly exhibit a train of signs and symptoms which permit a fairly easy diagnosis. Those with the milder affections are usually presented with a history of being late in holding up the head, sitting up et cetera. If the affection is more severe, the diagnosis is made earlier, as the spastic condition becomes obvious to the mother or nurse in bathing the child or adjusting the napkin. Still earlier, we may see the new-born

baby exhibiting stupor, and difficulty may be experienced in getting it to take its food. In these last cases, if a careful examination is made, some degree of spasticity will be found, masked, however, to some extent by the lethargy of the infant. The manifestations of the disease are varied, the classical picture being, of course, the spastic diplegia with the lower limbs more affected than the upper; attempts to flex the limbs passively reveal the spastic condition, and the tendon reflexes are found to be exaggerated, although in the very severe cases it may be difficult to elicit the reflexes at all. The spasm of the adductors, producing the typical scissors legs when attempts are made to move the lower limbs, is one of the most noticeable signs. The feet are usually held in the talipes equino-varus position, while the forearms are pronated with the thumbs across the palms. The face may be affected and there may be drooling of saliva, which may suggest mental deficiency,

¹ Read at a meeting of the New South Wales Branch of the British Medical Association on April 29, 1937.

although this is not always present. Other patients show a paraplegia only, and more rarely a single limb is affected or the condition may be hemiplegic. (In this connexion it is interesting to note the divergence of opinion as to the common type. Ryderberg, in Abt's "Pediatrics", states that the hemiplegic cases are three times as common as the paraplegic or diplegic, while Sheldon, in his recent book, "Diseases of Infancy and Childhood", notes the most common form as diplegia. My own experience shows this latter type to be more frequent.) In addition to the spasticity, abnormal movements may be shown, usually athetoid and more seldom choreiform. In the majority of cases of a fairly marked degree, and especially in young infants, some incoordination in swallowing is present, leading to great difficulty in feeding, and this is one of the conditions which brings the infant under the care of the physician.

Early recognition of the disease is, of course, desirable so that remedial measures may be instituted to prevent deformities and to establish as soon as possible some definite line of training for the spastic limbs. A careful estimate of the child's condition must be made, as the parent's first question is usually one as to the prognosis. In this regard, probably the most important point is the degree of intelligence of the child, and due weight must be given to the retardation that occurs in all children cut off from the normal stimuli of their environment. These spastic children lack ability to touch and grasp objects, to crawl about and to explore their surroundings; and this leads to a slowing of their mental development, even when no mental deficiency is present. The degree of spasticity found and parts affected have also to be taken into consideration, but it can be said generally that, while it is possible (in the absence of gross mental defect) to teach the child to walk, feed itself et cetera, it is unlikely to acquire ability to perform the finer movements of the hands; and, of course, if any added mental defect is present, there will be so much more difficulty in education and a somewhat lower standard of improvement.

The question of ætiology of the condition is most interesting and again reveals a divergence of opinion. It is quite commonly held that trauma, due to injury at birth, is the most common cause, acting by damage to the cerebral cortex from hemorrhage of the longitudinal sinus or from rupture of an artery or from tears and lacerations of the brain tissue following fractures and compression of the skull. This seems a reasonable explanation, especially when there is a history of prematurity, when the skull and its contents are more liable to injury owing to the greater compressibility and also because the capillaries are relatively more fragile; when there is a history of precipitate labour with sudden release of pressure on the head, which may cause tearing of the membranes; when there is a history of prolonged labour, when the head is unduly compressed, or perhaps of forceps delivery with frank damage to the skull.

Undoubtedly in cases with such histories brain damage does occur sometimes (manifesting itself by such phenomena as coma or convulsions) and may be followed by permanent damage to the cortex, with spastic paralyses, mental defect et ceters. It seems probable, however, that the permanent injuries are caused by bleeding from an artery and laceration of the brain substance; while tears of the longitudinal sinus, though causing coma perhaps in the early days, are more likely to clear up without leaving behind any spastic condition. The idea that the condition is most commonly caused by intracranial hamorrhage is the most frequently quoted in the text-books. On the other hand, it is interesting to note that Freud in 1901 said:

Since such injuries [birth trauma with meningeal hæmorrhage] are so frequently without effect, one cannot exclude the possibility that the existent diplegia is congenitally conditioned, in spite of Little's case histories and that, in certain cases, the difficult labour itself is only a manifestation of a deeper lying influence which has dominated the development of the fætus and the organism of the mother.

Grulee, in an article on intracranial hæmorrhage of the new-born in the American Journal of Diseases of Children of September, 1936, points out that Collier in 1924 said that after a review of Little's report on diplegia, he could find no evidence that Little in any case attributed the condition to intracranial hæmorrhage of the new-born. Collier, writing in Brain in 1924, after going carefully into the literature of the subject, stated that he could find no evidence to support the generally accepted notion that diplegia was frequently the result of such hæmorrhage, and concluded with the statement: "the evidence demands the verdict that meningeal hæmorrhage should be deleted as the causal factor in any infantile spastic state".

Ford, writing in *Medicine* in 1926, made a careful study of cerebral palsies and found that only 6% were due to injury at birth. He states:

Common diffuse meningeal hemorrhage, which is not large enough to cause death, apparently leaves no residuum, in an overwhelming majority of cases. The real birth injuries of the brain are caused by the irregular intra-cranial hemorrhages and necroses, by depressed fractures with laceration of the brain and undoubtedly by more or less encapsulated meningeal hematomas.

He further states that: "the diplegia is the result of a physiological process of intra-uterine origin", and is not due to hæmorrhage at birth.

Grulee himself, in the article referred to, after discussing these matters, sums up:

Even if the physicians arrive at some method by which they can materially reduce or even eliminate intra-cranial homorrhage of the new-born, they are sure to be disappointed in the results, because they still have to deal with those conditions which, in the past, have been erroneously attributed to this accident.

The discussion may seem academic, since the patients as we see them are suffering from spastic paralysis and there is no way of differentiating the cause, that is, whether the condition is due to a primary cerebral agenesis or hypoplasia or to injury at birth. But it is of real interest in that we may

be helped in prognosis in those neonatal cases of convulsions, coma et cetera if we can decide whether they are due to definite brain laceration. If laceration of the brain is the cause, some after-effects will probably be found; if the condition is due to bleeding from the longitudinal sinus, it is more likely that the condition will clear up without detrimental result.

The differentiation is of course difficult, but with a history of natural labour without gross signs of injury to the skull one might look for the quiet sinus hæmorrhage at low pressure, soon ceasing and leaving no permanent damage. At the other end of the scale, however, we have the frankly damaged skull with possible brain laceration and permanent injury. If we allow that the commoner cause of spastic paralysis is some agenesia or hypoplasia of the brain (and there seems to be a good deal of evidence in its favour) we shall realize that treatment from the first must rest on education of the spastic muscles. This of course is the province of the orthopædic surgeon, and the pædiatrician can help only by early diagnosis and by keeping the child's nutrition at the highest possible level, sometimes a difficult task owing to the incoordination in swallowing and lack of the stimulus of normal

THE SURGICAL TREATMENT OF SPASTIC PARALYSIS.1

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THERE is a confusion in the medical world regarding the exact meaning of the word spastic. English dictionaries give a variety of meanings, but the general view is expressed by the Oxford English Dictionary in which it is stated that a spastic patient is one performing involuntary contractile movements. Such movements are, however, known in medicine as choreiform, and we shall have to seek further for the true meaning of spasticity.

Now what are the characteristics of spastic paralysis seen in a patient suffering from congenital spastic paralysis of the lower limb? (i) A contraction of the extensor muscles of the whole limb and adductor muscles of the thigh in response to effort. (ii) A failure of reciprocal innervation, as shown by failure of antagonists to relax during the contraction of a particular muscle group. (iii) Resistance to passive movements in both flexors and extensors. (The characteristics (ii) and (iii) are not developed in very young children, but appear only as the diastolic blood pressure rises.) (iv) A characteristic knee jerk.

In the true spastic knee jerk there is: (a) an exaggerated phasic response as shown by the amplitude of extension of the knee, limited in older patients by failure of relaxation in the antagonists; (b) a prolonged relaxation time or postural

response due to the shortening reaction in the muscle. The leg does not oscillate when suspended. (This again is not seen in young children, but develops from the age of two or three years onwards.) This jerk is characteristic of true spastic paralysis, and the term should be reserved for the patients exhibiting its features. Very small children who have spastic paralysis may exhibit extensor spasm at first, and later develop the postural response in the knee jerk and resistance to passive movements.

A modified spastic knee jerk is seen in patients suffering from epilepsy, diabetes, Raynaud's disease and sometimes from thrombo-angiitis obliterans. These patients all have a raised diastolic pressure.

The Cause of Spastic Paralysis.

Spastic paralysis in the animal subject is due to a lesion of the premotor cortex, and it is probable that the same condition, as well as a lesion of the cerebro-spinal pathways, causes it in the human subject. The premotor cortex also controls the vasomotor centres, for a lesion of the area is followed by temporary cedema of the contralateral limbs and other evidence of vasomotor disturbance. (1)(2)(3)(4)

It is a common observation that the limbs of patients suffering from chronic spastic paralysis are cold and blue, indicating excessive constant constriction of the arterioles with consequent congestion of the blood supply. "Premotor animals, and certain human cases, as Gowers⁽⁶⁾ pointed out, show excess vaso-constriction—a difference which undoubtedly has localizing significance." For this reason the diastolic pressure of spastic limbs must be higher than that of normal limbs. In one instance I found the difference of 40 millimetres of mercury in the pressure of spastic lower limbs, when compared with the pressure of normal upper limbs. In another patient of nine years of age the diastolic pressure was 100.

The Relationship of Vasomotor Nucleus to Muscle Tone.

I have always insisted that the removal of the sympathetic nerves leads to a decrease in muscle tone. This sequence is inevitable, since the removal of the sympathetic nerves to the spinal cord and to the prespinal centres, after lumbar ramisction or superior thoracic ganglionectomy respectively, alters the circulation to these centres in such a way that the rate of capillary circulation is increased and gives oxygen less time to act; and consequently the activity of the nerve cells must be depressed, for nerve cells, including those of the respiratory centre, in common with most other cells, require oxygen for their activity.

This is not merely a theoretical consideration, for I have observed in the living animal after sympathectomy a dilatation of the arterioles on the side of the operation on the spinal cord. In addition, in the post mortem examination of the spinal cord there is seen a positive alteration of the blood supply, which is shown in Figure I. This must be

Read at a meeting of the New South Wales Branch of the British Medical Association on April 29, 1937.

due to an increase of rate of capillary flow, for the removal of the sympathetic nerves allows the arterioles and venules to dilate, with concomitant diminution of capillary calibre. In these circumstances the changes in activity of the lower motor neurones are inevitable, and the critics who failed to observe these changes must have erred in either their operations or their observations.

It is true that the prespinal centres contribute to muscle tone; but if the impulses from these centres fall on unsuitable ground, in the shape of depressed spinal centres, the result, as I have always insisted, must be obvious even in the decerebrate animal.

Under suitable vascular conditions, such as those in my experiments with the spinal animal under the influence of ephedrine, (7) it can be demonstrated that the spinal centres contribute to muscle tone. This is shown by the resistance of both flexors and extensors of the hind limbs of the goat under the influence of this drug. Ephedrine in large doses constricts the arterioles and venules, and this is (physiologically) accompanied by dilatation of the capillaries, which decreases the rate of capillary flow. The prespinal centres are known from Sherrington's work to be responsible for extensor tone, and I have shown that this extensor tone is depressed in the decrebrate animal on the contralateral side following a stellate ganglionectomy. (6)

There are thus two kinds of tone: one of the prespinal centres (extensor tone) and one of the spinal centres, which, by taking up the slack of resting muscles at the beginning of movement, assists the active contraction of both flexors and extensors.

Spinal muscle tone is thus a proprioceptive reflex action subserving active movement. It follows the beginning of active contraction, for there is no tone in resting muscle. Extensor tone is distinct and is an antigravity function of the nervous system, and is also proprioceptive in origin. It appears normally in muscles which are being stretched by gravity. The term muscle tone should be reserved for spinal tone.

Both mechanisms depend, however, on the sympathetic nervous system. The spinal tone depends on the decrease of rate of capillary flow round the anterior horn cells, and this is caused by constriction of the arterioles and consequent dilatation of the capillaries. It is probable that the proprioceptive impulses, in passing from the posterior nerve roots to the anterior horn cells, stimulate the vasomotor centres of the cord on the way. Thus the vascular conditions necessary for the activity of the nerve cells of the spinal cord subserving tone would be caused. The prespinal centres also depend on the sympathetic or vasomotor centre for decreased capillary flow associated with its hyperactivity. These are usually affected before the spinal centres, and their activity persists after the spinal centres are depressed.

The "release of function" following the cutting off of higher centres need affect the vasomotor centres only, as hyperactivity of these centres would provide the vascular conditions by constricting the

arterioles and decreasing the rate of capillary flow for the activity of other centres.

Spinal shock is a condition which follows division of the spinal cord, and is characterized by loss of function of the spinal centres. From what has been said above, the vascular condition of the cord must be an increase in capillary flow, owing to the hypoactivity of the spinal vasomotor centres when cut off from the controlling vasomotor centres in the medulla. The variable period of spinal shock is the period taken in the different animals for the spinal vasomotor centres to develop their autonomy. When their autonomy is as fully developed as it can be in an isolated cord, or when the stimulation from the vasomotor centres is excessive, as in spastic paralysis, the spinal centres overact, leading to vascular conditions subserving tone in centres of both flexors and extensors. This accounts for failure of reciprocal innervation in spastic paralysis.

The effect of increasing the capillary flow round the vasomotor centres following the operation of superior thoracic ganglionectomy on the spinal circulation is shown in Figures II and III. The ipsilateral effect is seen in the cervical region, and the contralateral in the thoracic region. The effect was seen seven weeks after the ganglionectomy in a goat which was killed by electrocution. It was anæsthetized before the current was passed, and death was instantaneous.

The Plan of Treatment.

Formerly I treated both spastic hemiplegia and spastic paraplegia by ipsilateral lumbar ramisection in the case of the lower limb, and ipsilateral sympathetic ramisection and later ipsilateral superior thoracic ganglionectomy in the upper limb. Since 1931 I have treated both spastic hemiplegia and spastic paraplegia by contralateral superior thoracic ganglionectomy, not because ipsilateral operations had no effect, for, in the words of R. B. Wade, (8) Past President of the Royal Australasian College of Surgeons, "the operation of ramisection (plus tenotomy and reduction) should be the operation of choice in the case of spastic paralysis", but because the removal of the spinal tone was masked by the persistence of extensor or prespinal tone. This is where my critics became confused in patients in whom prespinal tone persists. I would not hesitate to do a sympathetic ramisection for the lower limb as well as a superior thoracic ganglionectomy, but I have had to do it in three or four patients only to the present.

The Effects of Superior Thoracic Sympathetic Ganglionectomy.

The effects of superior thoracic sympathetic ganglionectomy are; (i) ipsilateral effects; (ii) contralateral effects.

Alteration of the Cerebral Circulation.—There is an acceleration in the rate of capillary flow in the cerebral circulation. This reduces the activity of the whole half brain to normal. It also reduces the action of hyperactive centres, leading to spasticity, to normal; for spasticity in the first place is due

to failure of inhibition from the premotor cortex, which affects probably the vasomotor centres.

Ipsilateral Effects.—A diminution of tone occurs in the muscles of the side of the face and neck and in the muscles of the same-sided upper limb. The size of the naso-labial fold is decreased and there is a partial collapse of the angle of the mouth on the same side and of the nostril of that side. In the conscious patient the sacro spinalis is slack at its attachment to the occiput.

Sluggishness in the Fall of the Eyelid on the Ipsilateral Side.—This is best seen with the patient under light anæsthesia. The eyelid droops slightly and the eye retracts after a superior thoracic ganglionectomy.

Contraction of the Pupil.—This phenomenon follows superior thoracic ganglionectomy. Even in deep anæsthesia the ipsilateral pupil is less dilated than the contralateral. On recovery from anæsthesia the patient exhibits a contracted pupil which is never pin-point in character, but has a diameter of two or three millimetres. In a moderately bright light in children the diameter may be three or four millimetres. These pupils react to light and may be dilated by atropine, but the dilatation is slower than in a normal eye. To my mind these phenomena indicate that there is some mechanism other than the sympathetic nervous system that is concerned in the normal dilatation of the pupil.

Cessation of Sweating.—This occurs on the ipsilateral side of the face and head and on the ipsilateral upper limb. It is not always permanent, for I have seen sweat appear on the face and upper limb of a patient suffering from hyperhydrosis after a superior thoracic ganglionectomy, and on the lower limb after a lumbar sympathectomy. I have also felt a small amount of sweat on the limbs of spastic patients after similar operations have been carried out.

Circulatory Changes.—The colour of the ipsilateral side of the face and upper limb changes after a superior thoracic ganglionectomy. It becomes paler than that of the contralateral side. If the contralateral ear is bluish, the ipsilateral shows a pinker shade. The colour of the contralateral lower limb in a few days' time is paler than that of the ipsilateral. This is undoubtedly due to the alteration in activity of the vasomotor centres of the cord.

A curious phenomenon, which shows that the control of the sympathetic nervous system is contralateral, appears in young children and sometimes in adults. This phenomenon is a scarlet blush which appears on the contralateral side of the face, owing apparently to an acute capillary dilatation. It is sharply marked off in the mid-line of the face and scalp. The blush fades in a few hours and is succeeded by pallor. This shows that the capillary dilatation follows depression of activity of the vasomotor nucleus, which is occasioned because its oxygen supply is less readily available through increased capillary flow. This is the result of

superior thoracic ganglionectomy, because this operation leads to dilatation of arterioles.

Temperature.—The temperature of the ipsilateral upper limb and side of the face is higher than that of the contralateral limb and side of the face. This effect is permanent and has been observed five years after sympathectomy.

Horner's Syndrome.

From the above description of the ipsilateral result of superior thoracic ganglionectomy it will be seen that the description of Horner's syndrome should be altered, for, in addition to the usually observed changes, namely, retraction of the eye, a contracted pupil and ptosis of the upper lid, there are changes in facial musculature. These changes are a loss of tone, and are due to the increase in capillary flow and consequent less availability of oxygen round the facial nucleus.

Contralateral Effects.

Contralateral Loss of Tone.—This is observed best in the lower limbs, for in the upper limbs there is a loss in tone in the ipsilateral as well as in the contralateral limb. The loss in tone is shown by the alteration in character of the reflexes. Both the prespinal or extensor tone and the spinal tone are depressed, as demonstrated by a return of the oscillatory type of knee jerk, there is also a diminution of the amplitude of the Babinski reaction. This is undoubtedly due to the change in cerebral circulation on the ipsilateral side and to the change in spinal circulation on the contralateral side.

Changes in Circulation.—The contralateral lower limb is always paler and warmer than the ipsilateral after a superior thoracic ganglionectomy. This indicates a greater rate of capillary flow, for the arterioles are dilated and the capillaries contracted.

Fall in Blood Pressure.—In spite of assertions to the contrary, there is a fall in blood pressure in the contralateral limb following a superior thoracic ganglionectomy. This affects primarily the diastolic pressure. The observations for the changes in blood pressure should be made on the lower limb. This fall in blood pressure again indicates that the spinal activity is depressed coincidently with a lower diastolic pressure, which must be the result of depressed activity of the vasomotor nucleus on the contralateral side following sympathectomy.

Contralateral Control of the Sympathetic or Vasomotor Nucleus.

I believe that the sympathetic nervous system does nothing except control the muscles of the blood vessels, and that the vasomotor nucleus is the sympathetic centre. From observations made above it is evident that the control of the vasomotor centres is contralateral.

Time for Operative Treatment.

Sympathectomy does not remove contractures, and the proper time to do the operation is before contractures develop; that is, as soon as the condition of spasticity manifests itself. This is usually in the second year of life.

Treatment of Contractures.

Subcutaneous tenotomy of the adductors usually suffices for adductor shortening, particularly if the limbs are plastered in abduction for six or eight weeks afterwards. Contractures of the hamstrings should be treated by open tenotomy. A warning must be given against division of the tendo Achillis in spastic paralysis to correct contractures of the calf muscles. A crippling deformity is the inevitable result, particularly if the feet are over-corrected and placed in dorsiflexion. This unfortunate deformity occurred in one of my early patients, and I have seen it many times in patients operated upon by other surgeons.

Reeducation in Spastic Paralysis.

The operative treatment outlined in this paper does not represent a final therapeutic measure. The patient must be physically educated. Children who have never walked cannot be expected to do so immediately, since it takes a normal child twelve or fifteen months to learn to walk. Even when the spastic patient has control of movement it is usually very defective. For example, the control of coordinated groups, such as in flexion and extension of a lower limb, may be present, but the separate control of each group of muscles may be entirely absent.

The First Consideration.

The first aim therefore is to establish group control, and in this process there are certain muscles which are more important than others. The sacrospinalis is the first to demand attention, for without this muscle the patient cannot hold the head and trunk erect in the act of standing. The next group is that concerned with the extension of the lower limb at the hips, namely, the glutous maximus. Many a child is condemned to a life of dependence because the gluteal muscles have not received attention. I include in the training the gluteus medius, without which the patient is unable to balance on one leg. This muscle acts in balance as a strap holding the pelvis down to the great trochanter.

It is in few instances only that some control of coordinated movement is not present in patients suffering from spastic paralysis. Inhibition of opposing groups is found to be effective after sympathectomy, and the process of education is then made easier. When the control of group movement has been acquired the patient should be taught to stand. Any patient who has control of the sacrospinalis and gluteal muscles, and ability to flex and extend the lower limb as a coordinated movement, may be made to stand.

The next step is to teach the patient to walk. A study of normal walk reveals that the forward lower limb takes the weight as the hindmost lower limb relaxes and falls forward ready for extension. The pelvis at the same time is held level. This differs from the spastic gait in that the patient carries the lower limb forward rigidly and lifts the same side of the pelvis as he goes. He endeavours

to bend the lower limb as a final act. This should be corrected and the patient instructed to bend and relax his lower limb as a preliminary to movement. In the upper limb in hemiplegic patients enclosure of the sound limb in plaster of Paris to force use of the defective limb is a sound procedure,

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FORMOL-TOXOIDS IN THE PROPHYLAXIS OF GAS GANGRENE.

By W. J. PENFOLD, M.B., Ch.M. (Edinburgh), D.P.H., B.Hyg. (Durham), M.R.C.S. (England), L.R.C.P. (London),

AND ...

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FROM a consideration of gas gangrene infections during the Great War, the Medical Research Committee(1) (1919) concluded that the three types of pathogenic anaerobes most concerned were Bacillus welchii, Vibrion septique and Bacillus ædematiens, and that of these Bacillus welchii had by far the greatest incidence.

Hill(2) (1936) reported a series of post-abortal septicæmias due to bacilli of the gas gangrene group. He showed (Table II) that of 17 such patients no less than 15 were infected with Bacillus welchii, while two were infected with Vibrion septique. Of four puerperal septicæmias caused by bacilli of the same group, all were due to Bacillus welchii. Combining the two series we have 21 cases of septicemia due to bacilli of this group, of which 19 were caused by Bacillus welchii. Of se 19 patients, 11 died. Of the two patients with Vibrion septique, one died. It is evident, therefore, that in the septicemias due to the gas bacilli that occur in obstetrical and gynaecological practice, Bacillus welchii plays a very important rôle. The

ILLUSTRATIONS TO THE ARTICLE BY DR. N. D. ROYLE.

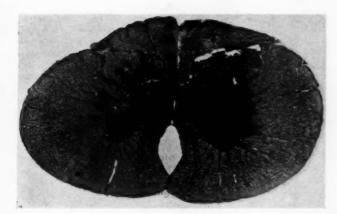


Figure I

Showing the vascular changes in the spinal cord after a left lumbar sympathectomy in a goat fourteen days after operation. It shows the effects of greater drainage on the ipsilateral side and congestion on the contralateral.



A section of the cervical cord showing the ipsilateral changes in vascularity following a right-sided stellate ganglionectomy. Note the congestion on the contralateral side.

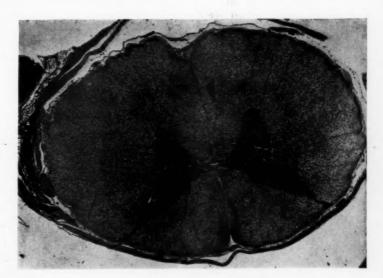
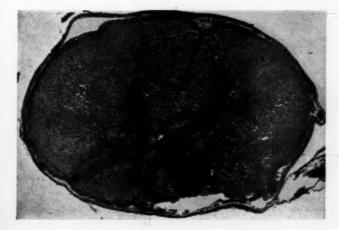


FIGURE III.

A section in the upper thoracic region showing the contralateral changes in vascularity following stellate ganglionectomy in a goat. Note the congestion on the ipsilateral side and free drainage on the contralateral.



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infections dealt with above all occurred in patients who were in the Women's Hospital, Melbourne, within a period of less than two years, namely, April, 1933, to February, 1935, so that the problem of gas bacillary infection is one of great magnitude and gravity.

The Nature of Bacillus Welchil Toxins.

Bull and Pritchett⁽³⁾ (1917) were the first to demonstrate a true exotoxin in *Bacillus welchii* cultures. Filtrates of cultures grown in meat broth containing 0·1% glucose were toxic for animals and the toxin was specific, thermolabile and antigenic.

Bull and Pritchett described the toxin as a complex of a hæmolysin and another poisonous body causing inflammation and necrosis of subcutaneous tissue and muscles. Later Henry⁽⁴⁾ (1923) gave the name of myotoxin to this necrosing substance. The stimulation of involuntary muscles by Bacillus welchii toxin was noted by the Medical Research Committee's workers⁽⁵⁾ (1919), and in 1928 Buttle and Trevan⁽⁶⁾ studied the action of the toxin on the isolated rabbit uterus and found that it caused spasmodic contractions in it. These contractions were inhibited by specific antitoxin.

Production of Toxins. Medium.

Tryptic meat broth was used for the production of our Bacillus welchii toxins. The broth portion is made according to Hartley's method(1) (1922), veal being used instead of horse muscle, and 10 cubic centimetres of Cole and Onslow's pancreatic extract instead of 5 cubic centimetres for the digestion of 500 cubic centimetres of the meat infusion. The mixture is incubated at 37° to 40° C. for five or six hours until the biuret test gives a positive result. After the addition of 40 cubic centimetres of normal hydrochloric acid, the mixture is steamed for half an hour, then cooled and filtered. The reaction is adjusted to pH 7.6, and 0.1% of glucose is added. Equal parts by weight of minced veal and N/20 sodium hydroxide solution are now mixed together and boiled for half an hour. The meat fragments are then freezed free of solution and added to the tryptic broth which is already distributed in flasks. The meat should occupy from one-quarter to one-third of the total volume of the medium. Liquid paraffin is placed on the surface of the medium, which is then sterilized by steaming for half an hour at 100° C. and autoclaving for half an hour at 120° C. The final reaction of the broth is from pH 6.8 to 7.2.

Strain.

The strain used in our experiments was obtained from the Mulford Biological Laboratories, Pennsylvania, United States of America, for which we desire to thank Dr. Reichel.

Toxin Production and Minimum Lethal Dose.

The inoculum was 20 cubic centimetres of a sixhour culture for seven litres of broth. The broth was warmed to 37° C., inoculated, and then incu-

bated at 37° C. for about eighteen hours. The purity of the culture was tested by making smears and subcultures. Cultures were filtered through Seitz asbestos filter pads, a clearing pad first being used to reduce the number of bacteria and then a bacterial pad to remove the residual bacteria. The sterility of the filtrates was tested in meat broth containing active trypsin and the toxicity was tested in mice. If 0.1 cubic centimetre of filtrate given intraperitoneally killed each of two mice within twenty-four hours, the filtrate was accepted as a good toxin. Smaller doses were frequently not tested, but we had some toxins which killed in 0.05 cubic centimetre and others in which the minimum lethal dose was as high as 0.25 cubic centimetre. The intravenous minimum lethal dose of a good toxin usually lies between the limits of 0.01 to 0.1 cubic centimetre for mice (Dalling et alii, (8) 1928; O'Brien, (9) 1929), and O'Brien quoted the intramuscular minimum lethal dose in different species as 0.3 to 1.0 cubic centimetre for the mouse, 0.2 to 1.0 cubic centimetre for the pigeon, and 0.2 to 0.3 cubic centimetre for the guinea-pig. It has been our general experience that when the intraperitoneal route is used the rat is much more susceptible per gramme of body weight than the mouse. The detailed experiments recorded in Table I indicate this, but as between the rat and the guinea-pig our figures do not enable us to make a positive statement.

The Production of Formol-Toxoid from Toxin.

The preparations generally used for human immunization against diphtheria have been toxinantitoxin or toxoid-antitoxin mixtures of various strengths, toxin-antitoxin or toxoid-antitoxin floccules, toxoid alone, or alum-precipitated toxoid. The materials most in favour appear to be toxoid, alum-precipitated toxoid and toxoid-antitoxin floccules. Our early experiments were conducted to determine the possibility and the feasibility of using Bacillus welchii formol-toxoid as an immunizing agent. We have had in mind the regulations for the standardization of diphtheria toxoid or other similar prophylactic, as stated under the Therapeutic Substances Act (see Topley, (10) 1933). To ensure that the immunity produced was effective, we have tested our animals not only with toxin, but with several lethal doses of culture.

In 1904 Glenny (see Glenny and Hopkins, (11) 1923) used diphtheria toxin modified with formalin as an antigen for producing immunity in animals. In his early experiments the material was not completely atoxic, but some years later good antitoxin was obtained with a toxin so modified with formalin that 5 cubic centimetres would not kill a guineanim (12) 1921

Ramon⁽¹³⁾ (1923) also described the production of immunity with diphtheria formol-toxoid to which he gave the special name of "anatoxine". Tetanus formol-toxoid was used by Descombey⁽¹⁴⁾ in 1925 for the immunization of horses. Weinberg and Prévot⁽¹⁰⁾ (1925) and Welikanow⁽¹⁶⁾ (1931)

pig. (Glenny and Südmersen, (12) 1921.)

immunized animals with formalized cultures of Bacillus welchii, but Green⁽¹⁷⁾ (1929) was less successful. Mason, Ross and Dalling⁽¹⁸⁾ (1931) used formalized cultures of the lamb dysentery bacillus and of Bacillus paludis for the immunization of sheep.

Formalized cultures were called "anacultures" by Weinberg and Prévot(15) (1925), but there is some confusion in the literature because the term "anatoxine" is sometimes applied not only to the formalised culture-filtrate (the formol-toxoid), but also to the formalized culture. The use of formalized cultures in man is not feasible owing to the possibility of injecting live spores; hence we have concentrated our attention on formol-toxoids. Mason (1933) prepared antitoxins against Bacillus welchii, Bacillus paludis and the lamb dysentery bacillus by the subcutaneous injection of formol-toxoid followed by toxin. But the value of Bacillus welchii formol-toxoid alone as an immunizing agent has not apparently received much attention, and as far as we have been able to ascertain,

it has never been used in man.

Weinberg and Prévost⁽²⁰⁾ (1924) found that Baoillus welchii toxins to which 0·15% to 0·3% of formalin was added lost their hemolytic power and their toxic properties after incubation at 37° °C. for forty-eight hours. Injected in doses of 3 to 5 cubic centimetres in the thigh of a guinea-pig, they did not provoke any inflammatory reaction in most cases. Guinea-pigs injected with 3 to 5 cubic centimetres of formol-toxoid succumbed to a lethal dose of culture when tested after fifteen days. Weinberg

of culture when tested after fifteen days. Weinberg and Prevot were working with three different organisms, Bacillus welchii, Vibrion septique and Bacillus histolyticus. They stated that, using four different formol-toxoids, they gave 16 guinea-pigs two injections at eight and ten days' interval. Two of these were accidentally killed and did not show lesions. The remaining 14 were tested ten days after the second injection and all survived. As no further details were given and it is not clear how the animals were tested, we consider that there is no real evidence that immunity to Bacillus welchii infection was demonstrated. A good antitoxin was obtained in horses, however, by the repeated injection of formol-toxoid. Dalling and Mason (21) (1926) discussed the immunizing value of a formoltoxoid prepared from the toxin of an organism which they considered at that time to be Bacillus welchii. They were able to demonstrate the production of immunity in guinea-pigs to a certain lethal dose of the specific toxin. It is now clear that they were dealing with the lamb dysentery bacillus

Bacillus welchii.

Wilsdon⁽²²⁾ (1931) stated that toxins of classical Bacillus welchii at pH 6-5 became atoxic when incubated for three days at 37° C. in the presence of 0-1% formalin. Walbum and Reymann⁽²³⁾ (1933), using toxins at pH 6-3 to 6-6 and 0-4% formalin, found that it required three to ten days' incubation at 37° C, to reduce the toxicity to such

which is distinctly different from the classical

an extent that 0.5 cubic centimetre injected intravenously in mice caused no symptoms of intoxication.

Our experiments have been carried out with freshly prepared Bacillus welchii culture-filtrates of pH 6.2 to 6.5, of which the minimum lethal dose by the intraperitoneal route was 0.1 cubic centimetre or less for a twenty-gramme mouse. After the addition of about 0.35% of formalin the toxins were incubated at 37° C. Within five to seven days under these conditions the toxicity was so reduced that 1.0 cubic centimetre failed to kill mice intraperitoneally, and 10 cubic centimetres injected subcutaneously in guinea-pigs caused only a small local reaction. In two cases the decline of toxicity for mice was studied in detail. The minimum lethal dose of formol-toxoid "A" increased from 0.1 cubic centimetre to 0.3 cubic centimetre by the second day of incubation. On the third day it was 0.5 cubic centimetre, on the fifth day 0.8 cubic centimetre, on the sixth day 1.0 cubic centimetre, and on the seventh day more than 1.0 cubic centimetre. The minimum lethal dose of formol-toxoid "B" changed from 0.05 cubic centimetre to 0.3 cubic centimetre by the end of the first day, to 0.4 cubic centimetre by the third day, 0.6 cubic centimetre by the fourth day, 1 cubic centimetre by the sixth day, and on the seventh day 1 cubic centimetre failed to kill. These observations are in accord with those of Walbum and Reymann as to the rate of detoxification of Bacillus welchii toxoids, but they do not support the general statements of Weinberg and Prévost, nor of Wilsdon. The latter workers, however, did not show clearly to what extent toxicity for mice was reduced in their experiments.

In our later experiments the relative susceptibility of rats was discovered, when it was found that the formol-toxoids required twelve to thirteen days' incubation before the intraperitoneal injection of 5 cubic centimetres failed to kill rats of 100 grammes weight.

Immunizing Powers of Formol-Toxoids of Bacillus Welchil in Different Species.

Active Immunity.

Our early experiments in animals were made with formol-toxoids which were atoxic for mice in doses of 1.0 cubic centimetre intraperitoneally. These experiments were preliminary in character, conducted to ascertain whether toxoid immunity to Bacillus welchii infections was demonstrable. We found that such toxoid immunity is possible, but the number and size of the injections necessary to give a significant immunity indicated the need for much further work on the subject before it was permissible to conclude that the use of toxoid immunity was really feasible in the practical prophylaxis of Bacillus welchii infections.

Our experiments showed that 15 cubic centimetres of toxoid, given in two doses, appeared to protect two out of four guinea-pigs against two minimum lethal doses of Bacillus welchii toxin.

Twenty-nine cubic centimetres of toxoid, given in five doses, appeared to protect five out of six guineapigs against two minimum lethal doses of toxin. Combining these two results, we see that of ten animals which received toxoid, seven survived, while of the ten controls given the same dose of toxin none survived. Toxoid can apparently produce some immunity to Bacillus welchii toxin, but the quantities of toxoid were large.

Five bi-weekly injections of formol-toxoid protected only two out of four guinea-pigs, and six injections protected three out of four guineapigs against 0.7 cubic centimetre of culture subcutaneously. In each experiment four control animals succumbed to 0.7 cubic centimetre of culture. When the sixth immunizing injection consisted of alum-precipitated toxoid given five months after the fifth injection of original formol-toxoid, four out of four guinea-pigs withstood 0.7 cubic centimetre of virulent culture, while four controls which had a smaller dose of culture (0.5 cubic centimetre) all died. Similarly four guinea-pigs which had seven injections of formol-toxoid and one injection of alum-precipitated formol-toxoid were protected against 0.7 cubic centimetre of culture, while the four controls failed to survive 0.5 cubic centimetre of culture. When 12 to 17 cubic centimetres of formol-toxoid were given in two and three injections respectively, only two out of four guineapigs in each group withstood virulent culture.

Six mice were given five injections of formoltoxoid (a total of 2.9 cubic centimetres) and withstood two minimum lethal doses of toxin when tested three weeks later. The six controls having the same dose of toxin, and two controls having half the dose of toxin all died. A similar group of five mice was tested with virulent culture three and a half months after the fifth injection of toxoid and all survived, while the five control mice succumbed to the same dose of culture.

We also demonstrated immunity to culture in four out of four rats following four large injections of toxoid, a total of 14-5 cubic centimetres being given to each animal. All four control rats receiving the same dose of culture died.

We have found that when formol-toxoids are incubated after they have been rendered atoxic for rats they rapidly lose antigenic power. We have failed to produce a significant immunity with such toxoids

Since five or six large doses were not feasible in practical prophylaxis in man, we attempted to increase the antigenic power of our formol-toxoids by precipitation with potassium alum. In 1926 Glenny, Pope, Waddington and Wallace (24) described the precipitation of diphtheria toxoid with alum and found that such precipitates had antigenic properties of high degree. In 1930 Glenny (25) found that the immunity produced by alum-treated diphtheria and tetanus toxoids was very much greater than that produced by toxoid alone. He ascribed this effect to the slow rate of absorption of the alum precipitate and the consequent prolongation of the antigenic stimulation. Glenny also found that Bacillus welchii toxins to which alum had been added were good immunizing agents. Since the publication of the work of Glenny and his co-workers on the immunizing value of alum-precipitated toxoids, the method has been widely applied and alum-precipitated formoltoxoids have been used with success as a means of immunizing children against diphtheria (Wells et alii, (26) 1932; Park, (27) 1935; Chesney, (28) 1936; Parish, (29) 1936).

An account of the precipitation of tetanus toxoid with alum was given by Jones and Moss⁽³⁰⁾ (1936). Guinea-pigs injected with one dose of one cubic centimetre of a suspension of precipitated toxoid showed six weeks later more than one unit of antitoxin per cubic centimetre of serum. In the human

TABLE I.

	Experiment (Tuxin Pebruary	iment I. Hary 2I, 1986.) (Toxin January 6,			I. Experiment III. (Toxin January 26, 1937.)		
Species.	Dose per Gramme Injected Intraperitoneally.	Fraction Died.	Dose per Gramme Injected Intraperitoneally.	Fraction Died.	Dose per Gramme Injected Intraperitoneally.	Fraction Died.	
White mice	0·004 0·006	3/8 4/4	0·002 0·003	0/4 4/4	0-008 0-0035	1/4 2/2	
Vhile zats	0-0007 0-0011	1/6	0-0010 0-0012 0-0015	0/2 3/4 4/4	=	Ē	
Philar rate	Ξ.	Ξ	0·0010 0·0012 0·0015	0/4 4/8 6/6	0-0010 0-0012	0/4 2/4	
Fulnos-pigs () p	0:0014 0:0020	2/4	0-0012 0-0015	3/2	0.0008	3/1	

The denominator of the traction indicates the total number of animals used in the particular experiment, and the numerator indicates the number of animals that died.

Doses of toxin are stated per gramme of body weight.

Species.	Experiment I.	Experiment II.	Experiment III.				
Mice	Grammes. 24 132 302		Grammes. 19 113 497				

subject immunization resulted in the production of at least one-twentieth of a unit of antitoxin in all but one of twenty-eight students receiving two injections, while of thirteen students who had three injections, none showed less than one-twentieth of a unit per cubic centimetre of serum. This immunity was greater than that produced with unprecipitated toxoid. The unit referred to was the American unit of antitoxin.

The technique adopted by Jones and Moss has been followed by us in the precipitation of Bacillus welchii toxoids. A preliminary titration was made by adding varying volumes of a 10% solution of alum to 10 cubic centimetre volumes of toxoid. The accompanying diagram represents a typical titration, in which the maximum precipitate was obtained with 0-8 cubic centimetre of 10% alum solution.

Number of Tube.	1	2	8	4	5	6	7		9	10
Cubic centimetres of alum solution	0.5	0-7	0.8	0.0	1.0	1-2	1.5	2 .0	5.0	7-0
			11.4							13
		[tal			1- (A)	11/14	1910 5 6 7	1000		
		90	100			Will !				
Amount of Precipitate				- 69			11.11			
			TW.				36			

One hundred cubic centimetres of a toxoid, "E", which was atoxic for mice in 1 cubic centimetre quantities but not for rats in 5 cubic centimetre quantities, were precipitated with 8 cubic centimetres of sterile 10% alum solution and after standing four hours at room temperature the supernatant fluid was removed. The precipitate was washed by adding normal saline solution and allowing the suspension to stand at room temperature overnight. After washing a second time the supernatant fluid was removed and the final volume of the suspension was brought to 25 cubic centimetres with sterile saline solution. No antiseptic was added in this case, as the material was for use in animals only.

In a similar manner 100 cubic centimetre volumes of the toxoid were precipitated with 5, 12, 20 and

50 cubic centimetres respectively of 10% alum solution. Groups of four guinea-pigs were given two injections a month apart, of the different suspensions in doses of 1.5 and 2.0 cubic centimetres (at least 60 and 80 mouse minimum lethal dose equivalents) and were tested with culture two to five weeks later. The results are given in Table II. They show that with the use of 5 cubic centimetres or 8 cubic centimetres of alum solution per 100 cubic centimetres of toxoid effective immunizing agents were obtained, while the increase of alum solution to 12, 20 and 50 cubic centimetres was associated with a fall in the immunizing value of the preparations.

One mouse minimum lethal dose equivalent represents the combining power of that fraction of toxoid which was recovered from one minimum lethal dose of the original toxin. This term is purely provisional and simply deals with the amount of toxin with which we started. Since the minimum lethal dose determined was only an approximation, the number of mouse minimum lethal dose equivalents in a particular dose of toxoid is never stated precisely, but rather as not being less than a given number. When the value of the toxoid as an immunizing agent has been demonstrated in the human subject, we hope to develop an exact method of expressing its binding power.

Another formol-toxoid which had been incubated until it was atoxic for rats in 5 cubic centimetre quantities intraperitoneally, was precipitated with alum in the zone of maximum precipitation, and a number of groups of guinea-pigs were given two injections one month apart, the largest doses being 1-5 and 2-0 cubic centimetres (not less than 159 and 212 mouse minimum lethal dose equivalents) and the smallest 0-2 and 0-5 cubic centimetre (at least 21 and 53 mouse minimum lethal dose equivalents). We were unable to demonstrate immunity to culture in any of these groups. This may have been due to the total destruction of the binding power of the toxoid, so we are inclined to think that atoxicity for rats in 5 cubic centimetre quantities is too severe a test.

We repeated our earlier experiment with a third formol-toxoid, "M", which was atoxic for mice in 1 cubic centimetre quantities intraperitoneally, but not in 5 cubic centimetre quantities for rats. It was precipitated with alum in the zone of maximum precipitation and the washed precipitate was suspended in one-ninth of the original volume. In this case 1 cubic centimetre contained the equivalent of at least 90 mouse minimum lethal doses. Groups of guinea-pigs, rats and mice were given two injections a month apart and were tested with culture a fortnight after the second dose. Detailed results are set out in Table III. Section 1 of that table shows that of eight guinea-pigs each inoculated with two small doses of alum-precipitated toxoid, all the eight survived when inoculated subcutaneously with 0.0015 cubic centimetre of culture per gramme of body weight. Of eight normal guinea-pigs given the same dose of culture, all died; of four guinea-pigs

TABLE II.

Section of the second		is another	Alum-precipitated	Formal-tereid E.		August (
Number of Group.	Cubic Centi- metres of Alum Solution used per 100 Cubic Centimetres of Toxoid,	Date of Test.	Number of Animals Tested.	Test Dose (Cubic Centimetres).	Number Survived.	Fraction Survived.
Test guinea-pigs,	5	15 7/36 22/7/36	1 8	0.7 of culture subcutaneously. 0.7 of culture subcutaneously.	1	3/4 •
2	8	92/7/36 29/7/36	1 2	0.7 of culture subcutaneously. 0.7 of culture subcutaneously.	. 1	8/8 †
8	12	29/7/36	1 2	0.7 of culture subcutaneously. 0.7 of culture subcutaneously.	1 0	1/3
	20	29/7/36 5/8/36	1	9-7 of culture subcutaneously 9-8 of culture subcutaneously	0	0/2
	50	15/7/86 5/8/30	1 1	0.7 of culture subcutaneously 0.3 of culture subcutaneously.	0	0/2
		15/7/38	1 1	0.7 of culture subcutaneously 0.3 of culture subcutaneously. 0.2 of culture subcutaneously.	0	0/8
Controle.		22/7/36	3 3	0-2 of culture subcutaneously. 0-1 of culture subcutaneously.	0	0/6
		29/7/36	3 3	0.2 of culture subcutaneously. 0.1 of culture subcutaneously. 0.05 of culture subcutaneously.	0 0 0	0/9
	23 13	5/8/36	3	0.05 of culture subcutaneously.	. 0	0/8

* In this group the animal which died survived for seven days after the test dose, while all six controls (July 22, 1936) were dead within two days, † A fourth animal in Group 2 was used as a source of serum which was found to contain one-fifth of a unit of antitoxin per cubic centimetre.

given half the quantity of culture, only one survived; and of four other guinea-pigs given one-tenth of the quantity of culture per gramme of body weight, again only one survived. The two small doses of toxoid had produced an excellent immunity against virulent culture and probably had protected against at least ten minimum lethal doses of it, one minimum lethal dose being taken as the least amount which will kill 50% of normal animals of standard weight. A more exact evaluation of the minimum lethal dose of culture was not attempted, as it would have required more animals than we could spare.

Section 2 of Table III shows that two small inoculations of alum-precipitated *Bacillus welchii* toxoid effectively protected rats against virulent culture, and Section 3 shows the same for mice.

These results confirm those given in Table II on the immunizing value of formol-toxoid "E" when precipitated with alum. It will be seen in Table II and in Sections 2 and 3 of Table III that not all the animals in a particular group were tested on the same day. This method was used so as to obtain an indication of the immunity produced in the group of animals and, as shown in the tables, each portion of an experiment was separately controlled with a number of normal animals.

Passive Immunity.

The mixed sera of two guinea-pigs which had received two doses of at least 75 and 100 mouse minimum lethal dose equivalents of alum-precipitated formol-toxoid were titrated by the intradermal method in guinea-pigs and found to contain more than 1-5 current American units of antitoxin per cubic centimetre. Passive immunity was demonstrated by injecting four mice with 0-8 cubic centimetre of this guinea-pig serum and twenty-four hours later injecting a certain lethal dose of culture. All four mice were protected, while four control mice without serum and four mice with the same quantity of normal guinea-pig serum died overnight from the same dose of culture.

Other Types of Bacillus Welchil.

In 1931 Wilsdon (22) studied the characteristics of 52 strains of organisms related to Bacillus welchii, and by cross-immunity experiments he was able to find amongst the 27 toxic strains four types, A, B, C and D. Of these, type A is the classical Bacillus welchii, type B represents the lamb dysentery bacillus of Dalling (31) (1928), type C is Bacillus paludis (McEwen, (32) 1930), and type D was subsequently shown to be the same as Bacillus ocitoxicus of Bennetts (33) (1932) (see Wilsdon, (34)

TABLE III.

Section.	Subjects.	Number in Group.	Number of Injustions.	Volume of Injections in Cubic Centi- metres,	Mouse Minimum Lethal Dose Equi- valents,	Date of Test.	Number Tested.	Test Dose per Gramme of Body Weight in Cubic Centimetres.	Number Survived.	Fraction Sarvived
I.	Test Animais.	:	2 2	1.5 2.0 1.0. 1.2	135 180 90 108	18/12/86 18/12/86		0-00015×10 of culture S.C. 0:00015×10 of culture S.C.		4/4
Guines-pign.	Controls.	4 8						0-00015 of culture S.C. 0-00015×5 of culture S.C. 0-00015×10 of culture S.C.	1 1	1/4 1/4 0/8
	Test Animais.	4	2	0·5 0·8	45 78	22/12/36 23/12/36	1 8	3-0 of culture S.C. 3-0 of culture S.C.	1)	.6/4
II. Ruts.	Controls.	7	ę ·			22/12/36 23/12/36	2 2 2 2	8 0 of culture 8.0. 2 5 of culture 8.0. 3 0 of culture 8.0. 2 5 of culture 8.0. 2 25 of culture 8.0.	0 0 0 0 0 1	0'4
	Test Animals.	5	*	0·25 0·5	92 45	17/12/86 21/12/86 22/12/86	1 8	0-3 of toxin T.P. 0-3 of toxin I.P. 0-4 of culture S.C.	1 }	2/2
III.	Controls.	8		×		17/12/36 21/12/36 22/12/36	9 9 9 4 9	0-3 of toxin I.P. 0-1 of toxin I.P. 0-3 of toxin I.P. 0-16 of toxin I.P. 0-4 of culture S.C. 0-2 of culture S.C.	0 0 0 0 0 0 0	0/8

I.P. - Introperitoneally.

S.C. = Subcutaneously.

1932-1933). Further important work on the toxins produced by the different types was published by Glenny and his co-workers^(ab) (1933). Since, as far as we have been able to ascertain, the types B, C and D, although infective for sheep, have not been shown to be the cause of gas gangrene in man, we have concentrated our efforts on the classical Bacillus welchii (type A). Experiments are in progress, however, to determine whether the inclusion of the antigens of these animal types would increase the protective value of our formol-toxoids.

Summary.

1. Formol-toxoids of Bacillus welchii which have been rendered atoxic for mice in one cubic centimetre quantities intraperitoneally produce effective immunity in animals when given in from four to eight large injections.

 Suspensions of alum precipitates of similar formol-toxoids given in two small injections a month apart are excellent immunizing agents in animals. Both active and passive immunity have been demonstrated.

The purpose of this research was to determine whether the prophylaxis of gas gangrene in man by the use of formol-toxoid was a feasible proposition or not. Our animal experiments suggest that it is, and at an early date we hope to apply it experimentally in man. If the experiments should

prove successful, the indications for the use of the prophylactic would probably be, firstly, in the army, particularly for contingents fighting in Europe, where the highly manured soil is frequently a source of infection; secondly, in women before the commencement of their child-bearing life or, alternatively, in women about to have abortion induced for any legitimate indication; and thirdly, for persons who take the risk of serious accidents, such as from farm machinery, motor-racing and the like. The use of serum therapeutically in such persons may induce serum-sensitiveness, with its attendant risks, which could be avoided if active immunization were carried out.

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When commencing this work we approached various authorities abroad for information on formol-toxoid made from Bacillus welchii toxin and for cultures of Bacillus welchii and related types, and obtained help in one or other or both of these ways from Professor Neufeld and Professor Dr. R. Otto, of the Robert Koch Institute, Berlin; Dr. H.

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PERIPHERAL VASCULAR DISEASE.

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This article is inspired by the number of cases of peripheral vascular disease that I have seen in recent years. I have read much of the literature bearing on the subject, and have begun to see some gleams of light, where formerly my knowledge was somewhat fragmentary. There is still, however, much to be cleared up, particularly in the ætiology and pathology of some of these affections. The treatment has been improved by the addition of operations on the sympathetic nervous system, but this improvement has not in many cases been permanent; thus much disappointment has been caused. It has been suggested that biochemical changes resulting in the formation of the so-called H-substance in the skin is the pathological factor in some of these affections.

In a subject that is still so abstruse, it is inevitable that I should have to rely for my information upon such authorities as Fraser, (1) Lewis, (2) Pickering, (8) and (in thrombo-angiitis particularly) upon Samuels,(4) of New York, whose experience in that disease has been unique. I have drawn liberally upon their communications in an endeavour to give a more scientific presentation of the subject.

I do not pretend that this article is an exhaustive account of the circulatory affections of the extremities; if it were it would include (amongst

others), in addition to those I mention: (a) The limbs that have received gunshot and other injuries affecting the nerves and vessels. (b) The vascular changes of amputation stumps. (c) Changes in limbs that are affected by anterior poliomyelitis. (In passing I would mention that I was able to convert a cold limb, that was partly paralysed as the result of anterior poliomyelitis some years before, into a much more comfortable, warm arm by lumbar sympathectomy.) (d) Affections of the veins.

ANATOMY.

Arterio-venous anastomoses (between arterioles and venules) are encountered especially in the palms of the hands and soles of the feet. They are particularly numerous at the ends of the digits; these are the site of a profuse distribution of sympathetic nerve fibres. These channels dilate as a reaction to: (a) mechanical stimulation, (b) histamine, (c) acetyl-choline, (d) cold. These anastomoses probably play a significant part in the vascular reactions of the skin of the hands and feet. They contract in the presence of adrenaline.

PHYSIOLOGY.

When the means by which dilatation and contraction are secured fail, we have the discomfort or disaster of disease. What are the means? The mechanism functions in response to: (a) variation in the temperature of the body or the surrounding medium, (b) physical influences, for example, gravity and pressure. Vaso-constriction is the result of the stimulus conveyed to the blood vessels along the sympathetic nerve fibres. It may originate in several ways: (i) Emotion (a) relayed direct from a centre in the thalamus, (b) indirectly through activation of the adrenals, (ii) Mostly it is the result of a peripheral stimulus conveyed by afferent nerves to the spinal cord, to rami communicantes, to the sympathetic ganglia, thence to the ultimate vascular distribution (either travelling by mixed nerves and leaving at intervals, they pass to the vessels, or, as some teach, by the outer coats of the larger arteries and so to the ultimate reaches of the vessel).

Vaso-Dilatation.-The influences which induce vaso-dilatation are not yet fully known. (a) It may be due to an inhibition of the vaso-constrictor impulse. (b) It has been claimed that a parasympathetic stimulus secures vaso-dilatation. (c) It may occur in response to a biochemical action (damage of skin will result in the release of a biochemical product to which the name of H-substance has been given; it has a resemblance to histamine and to acetyl-choline. It acts (i) by its direct effect upon the arteriole capillary wall, (ii) by a reflex from the dermal sensory nerves along the collateral twigs (ramifying in the arterio-venous anastomosis).

Skin Reactions in Response to Cold .- A low temperature is one of the most constant factors in initiating the vascular changes which constitute disease. In a normal limb cold produces a series

of reactions which resemble in some degree the changes of the diseased state.

I undertook the following tests at the Royal South Sydney Hospital last winter. Each experiment was conducted over fifteen minutes; iced water was used, the hand being immersed to the wrist.

- 1. At 60° F. slight pallor was present; there were no subjective symptoms. Signs of reaction were slow in appearing.
- 2. At 50° F. there was early cyanosis, which continued to the end of the experiment; the cyanosis was more evident on the dorsum of the hand. Slight tingling was
- 3. At 40° F. there was some initial pallor, then after five minutes both the palmar and dorsal aspects of the hand up to the wrist became bright red; the fingers became numb and clumsy.

The changes at 60° F. are due to a diminution of the blood supply to the area, the result of vasoconstriction; the stimulus is conveyed from the skin by the sensory nerves, thence to the peripheral vessels by the sympathetic.

At 50° F. the cyanosis is probably due to a capillary and arterio-venous dilatation, due to the release of H-substance from the deep layers of the skin. As there is associated contraction of the arteriolesthe result of a sympathetic stimulus—the rate of blood flow in the capillaries tends to fall, but as oxygen exchange continues, the carbon dioxide content of this portion of the circulation rises to an unduly high level. This explains the cyanosis.

After the initial pallor at 40° F. there is a bright red coloration. This phenomenon has been shown to occur independently of sympathetic nerve control. Some believe it to be the result of release from the skin of H-substance. The bright red colour (in contrast with the cyanosis at 50°) is thought to be due to the fact that the oxygen exchange is interrupted, and blood which is saturated with oxygen trickles through the dilated capillary field. Blisters are due to leakage of serum through a damaged capillary endothelium, from the prolonged cold.

CLASSIFICATION OF PERIPHERAL VASCULAR DIBEASE.

The following is a classification of peripheral vascular disease. The classification is partly taken from Fraser.

- A. The capillary group (including with the capillary the anastomotic arterio-venous channels).

 - The cold, blue extremity, or acrocyanosis.
 The red, cold and painful extremity—erythromelalgia.
 - Erythrocyanosis
 - 4. Frost-bite, trench-feet.
- B. The arterial group, in which it is possible to demonstrate changes in the arterial wall.
 - 1. Spasmodic.
 - Inflammatory. 3. Degenerative.

There are conditions simulating vascular disease, for example, the intermittent claudication which may appear in patients suffering from severe anemia; exercise of their limbs may cause severe muscular pain; cure 30f the anæmia generally abolishes the pain.

THE CAPILLARY GROUP OF VASCULAR DISEASES.

The capillary group of vascular diseases occurs mostly in females.

Acrocyanosis or Chilblains.

The usual story told by a patient with chilblains is that as a result of exposure of the hands or feet to cold the skin becomes a deep blue colour. If placed in warm water or in front of a fire, the part becomes warm and red; burning pain is felt and swelling occurs; red and intensely itchy patches appear. These changes bear a resemblance to the features which arise in the normal hand when it is subjected to the cold of 50° F., with this difference, that they arise at a temperature which would have little or no effect on the normal hand. In certain individuals the skin areas of the hands and feet are peculiarly sensitive to the effect of cold, with the result that a stimulus which in the ordinary individual would have little or no effect, induces in them an increased reflex, and at the same time the production in undue amount of the H-substance. The result is a contraction of the arterioles owing to an increase in their tone and a dilatation of the capillary field secondary to the effect of the H-substance. The blood is sluggish in its progress, yet parts with its oxygen and acquires an increased amount of carbon dioxide. These probably explain the cold, blue hand in a skin unduly sensitive to the influence of cold.

Treatment.—Protect the part from cold, Exercise the fingers or toes. Sulphur ointment applied to the skin and "Collosol" sulphur, two to five cubic centimetres injected intravenously, have been suggested as a prophylactic. Glycerine and belladonna, and ichthyol are amongst the numerous substances used for their relief. Rarely is more than this required. Periarterial sympathectomy, which partially relieves arterial constriction, has given some satisfaction in acrocyanosis. But as much of the pathology depends upon a biochemical influence exerted upon the capillary area, the results are not brilliant.

Erythromelalgia.

Lewis (2) concludes that there is no specific disease "erythromelalgia", but that a number of distinct types of patients present a peculiar state of the skin for which the term "erythralgia" is suggested. The condition is a painful redness of the skin, which is often, perhaps always, inflammatory. Owing to a toneless condition of the minute cutaneous vessels, the colour of the skin deepens greatly when the limb hangs down; this effect is not vasomotor in origin, but merely hydrostatic.

Erythrocyanosis.

Although not mentioned by Fraser, there is an affection of the peripheral vessels known as erythrocyanosis. It is the subject of a communication by Telford and Simmons in The British Medical Journal of March 28, 1986. The condition is one of reddish discoloration of the skin seen in the lower

half of the leg in girls and young women, especially just above the malleoli. (Acrocyanosis affects the most peripheral parts of the circulation—the digits, the ears and the nose.) The patients are of a stout and florid build and their limbs contain excess of fat; from time to time fairly large and distinct nodules appear in the subcutaneous tissue; they occasionally ulcerate.

Telford and Simmons consider that the vascular lesions in severe anterior poliomyelitis are clinically identical with those in erythrocyanosis. They ascribe it to a deficient blood supply, more especially a deficient venous return, in a loose unsupported fatty area far out in the peripheral circulation and exposed to cold. There is a striking resemblance on both clinical and pathological grounds between the nodular lesions and those of fat necrosis.

Treatment.—Telford and Simmons treated ten cases by bilateral lumbar ganglionectomy with most satisfactory results.

Frost-Bite.

Frost-bite results from the action of a prolonged exposure to extreme cold on the exposed tissues. It may arise either from the direct effect of cold on the tissues, when the process is painless and the waxy appearance of the affected tissues is usually first noticed by onlookers, or from the inflammation consequent upon thawing of the part, which, though frozen, has not been irretrievably chilled; this variety is extremely painful.

variety is extremely painful.

The pathology of the latter condition is that the prolonged anæmia from vaso-constriction so depresses the vitality of the tissues that the readmission of the circulating blood is followed by an acute inflammatory process, the resulting exudate being so excessive as to compress and thrombose the damaged vessels. For this reason restoration should be gradual and should be brought about by such means as by rubbing with snow and never by approaching near a fire.

Under this latter group of frost-bite is included "trench-feet".

In civilian life the only severe form of frost-bite I have seen was in a photographer, who, in ascending 10,000 feet or so over Sydney to take some infrared pictures of the Blue Mountains and beyond, omitted to keep his gloves on when changing the plates. He responded well to diathermy.

In the first stage the feet feel like pins and needles and "go to sleep". Later they swell, become red and tender and the circulation in them is sluggish. In the second stage the feet are swollen and cold; there is loss of sensation. The ædema does not pit on pressure as it does in the first stage. In the third stage gangrene appears.

Hughes⁽⁶⁾ came to the conclusion that there were two factors at work producing trench-feet, namely, a predisposing factor, fatigue, and an exciting factor, which is purely mechanical, namely, venous stagnation with consequent exudation of material into the tissues of the foot. The first stage is the stage of congestion; the second stage is the stage

of coagulation, in which there is no pitting on pressure; the third stage or the state of gangrene is brought about by the pressure of the exuded material on arteries and veins. There is thrombosis in the smaller venules. In his, Hughes's, opinion the main points in prevention are: (i) To keep the feet raised whenever possible so as to prevent stagnation; (ii) to give hot and nourishing food; (iii) to change the socks and to rub the feet.

In the Number 2 Australian Casualty Clearing Station we saw a good many cases of trench-feet in Flanders, in the winter of 1916-1917 particularly. For its treatment one of the medical officers (Allester), with the aid of the X ray technician, constructed a high-frequency outfit at a cost of about twelve francs (nowadays it would be called a diathermy machine and would cost thirty or forty guineas). This, in the opinion of Soltau, the consulting physician to the whole five British armies for this complaint, gave more relief of the pain than anything else he saw. This was very pleasing considering we were merely in a field in Flanders. We demonstrated it at a meeting of the Second Army Medical Society, at Hazebrouck, early in 1917.

THE ARTERIAL GROUP OF VASCULAR DISEASES.

As already stated, the arterial group of vascular diseases are of three varieties, spasmodic, inflammatory and degenerative. To assist in discriminating between these, various tests are found to be of value.

The Reactive Hyperamia Test.-The reactive hyperæmia test was introduced by Moszkowicz, but owing to the fact that he failed to keep the body and limbs warm the test fell into disrepute until modified by Pickering,(3) of the Medical Research Council. It should be performed in a room of 70° F. or over, and if the patient is not already comfortably warm he must be made comfortable by warming him with hot water bottles and blankets. If the upper limbs are being examined, the patient may be sitting; if the lower limbs, then he should be lying down. The limbs are warmed by immersing them for ten minutes in water at 95° F.; they are then lifted high out of the water in order to make the skin pale and the circulation is abruptly arrested by inflating to above systolic pressure a sphygmomanometer cuff wrapped around the upper arm or thigh. The limb is returned to the waterbath, and after four and a half minutes is lifted out, laid horizontally in a good light and dried; it should still be pale. A half minute later the circulation is released and the course of the flush is observed. When the vessels are patent, that is, in normal subjects and patients suffering from uncom-plicated Raynaud's disease and acrocyanosis, the flush reaches the tips of the digits in less than five seconds, is bright in colour, and reaches a maximum intensity in fifteen seconds or less, and fades quickly. In subjects with structural disease of the vessels the flush fades slowly and in patches, and may not appear in the tips of the digits until a minute or more after circulatory release. In these

cases, too, the flush is commonly a little cyanotic in tint and often lasts for a very long period of time.

The test may be performed upon a bedridden patient, the limbs being kept warm by covering them with blankets and hot water bottles. The test is of some value in selecting the lowest safe site for amputation if some arbitrary time limit for the appearance of the flush is set that is compatible with the healing of such skin when cut into flaps. It is suggested that if a bright flush appears in the heel within fifteen seconds of circulatory release, then amputation just above the ankle is safe, and if the flush appears in the toes within twenty seconds then amputation of the toes is likely to be successful.

In my experience over the last three years I can confirm Pickering's contention that the reactive hyperæmia test is the simplest and most reliable one for identifying structural disease of the vessels and should supplant the older and more complicated methods.

I have used it in all varieties of cases in which there was no suspicion of vascular disease and have found the hyperæmia to come within the normal period, namely, five to fifteen seconds. I have also used it in many cases of Raynaud's disease, in which I found the time normal. In arteriosclerosis I found the time lengthened; it was lengthened up to one minute fifteen seconds in a man of seventy-eight who a little later had had his foot amputated for gangrene as the result of arterio-sclerosis.

In Buerger's disease I found the time invariably lengthened, even up to two minutes thirty seconds. In one case of this disease the result was even discriminatory; the time was twenty seconds in the fourth and fifth digits (in which there was no complaint of pain) and over sixty seconds with a patchy response in the second and third digits; in these there was intense pain, for which amputation had to be performed, the vessels showing marked changes of thrombo-angiitis obliterans.

Pulsation of Vessels.—Much stress is laid upon the absence of pulsation, in such vessels as the posterior tibial and the dorsalis pedis, as indicating Buerger's disease, but I hesitate to lay too much stress upon this, as in a large number of routine examinations I have not uncommonly found it difficult to detect pulsation in this situation in the arteries of some normal people.

Postural Changes in Skin Colour.—Conspicuous pallor of the skin when a limb is raised and maintained for a few minutes some distance above the level of the heart is strongly suggestive of a structural lesion of the vessels; and the height at which such pallor appears is used by Buerger as an index of the degree of disease. The extent of the collateral circulation is shown by the irregular advancing colour when the limb is placed in the dependent position. When the obstructive lesion is confined to the toes, cyanosis usually follows the return of the limb to the dependent position; and

the diagnosis of Raynaud's disease is sometimes erroneously made.

Temperature of the Limb.—Although it is the rule for a limb affected by structural vascular disease to be persistently colder than its fellow, the reverse is occasionally found. I have made no observations on the temperature of the skin's surface beyond those ordinarily made by touch. However, some observers use the thermo-couple.

Pachon's Oscillometer.—Pachon's oscillometer records pulsation of the arteries in situations such as the calf of the leg, where the vessels lie deep and are inaccessible to the finger. R. B. Wade has used it in several of my cases with moderate success.

The Effect on Skin Temperature of Removing Sympathetic Vaso-Constrictor Tone.—The effect on skin temperature of removing sympathetic vaso-constrictor tone, by such procedures as injecting "Novocain" around a mixed nerve or into the spinal canal, will serve as an indication to treatment. If a lesion is present in an extremity that is habitually cool, but which becomes warm during a test, then it is reasonable to anticipate some improvement to result from the removal of sympathetic tone. I have no experience of this.

Arteriography.—I have performed arteriography in seven or eight cases, injecting three cubic centimetres of lipiodol into the femoral artery, taking three or four minutes to make the injection. Others have used "Thorotrast".

Radiographs showed shadows in varying situations—in popliteal arteries, in the upper end of tibial arteries, also in the plantar vessels.

In one patient who had had a leg amputated elsewhere and whose pain in the other leg has been completely relieved for eight months, the lipidol injection went through without a shadow; pulsation was not very satisfactory in the posterior tibial and dorsolis pedis arteries; and I have reason to believe that he really was suffering from thrombo-angiitis obliteruns. The oscillometer showed the circulation about the time the arteriograph was taken to be good in the painful limb, but the reactive hyperemia test (performed a year or so later) revealed considerable prolongation of time. He was in and out of hospital frequently.

In another case X ray examination shortly after the lipiodol injection showed shadows at the upper end of the tibial arteries (also in the dorsalis pedis and plantar arteries); fifteen minutes later the shadows in the tibial vessels had disappeared, those in the foot remaining; five days later all were clear. The patient was definitely suffering from thrombo-angiitis obliterans.

Spaemodic Conditions of the Arterial Group of Diseases. Raynaud's Disease.

Raynaud's disease is the most typical of the spasmodic conditions of the arterial group of diseases. Lewis defines Raynaud's disease as "a malady in which the fingers and toes become periodically pale or cyanotic, and in which after many winters of repeated attacks the terminal portions of the digits may be lost by a process of dry gangrene". Adson states that separation of the two main forms of vasomotor disturbances is usually simple, if one recognizes that vaso-constrictor disturbances cause cold extremities and vaso-dilator disturbances cause warm extremities.

But there are many borderline vasomotor disturbances of the hands and feet that lack nomenclature, for example, the intermittent "dead finger", the cold, red hands most common in adolescent girls, and the paroxysmal cyanotic digits.

But to return to Raynaud's disease.

Sex.—The disease generally occurs in females; occasionally in them there may be some evidence of hormone disturbance, but this is not universal. One of my patients said that her trouble dated from puerperal sepsis after the birth of her second child some years previously. Another had had a laparotomy for some pelvic trouble many years before. Another one is suffering from menorrhagia and epigastric pain; another from dysmenorrhæa and chronic streptococcal gastritis (secondary to tonsils infected with streptococci).

Location.—The disease is generally bilateral, usually in the hands, but I have several cases in which all four extremities are affected. Geoffrey Bourne, (6) in his paper on cardiac pain, mentions the frequent association of spasmodic angina with Raynaud-like spasm of peripheral blood vessels.

Etiology.—The etiology is quite uncertain. Cold is the undoubted exciting cause; the disease lasts longer, for example, in Melbourne than in Sydney, on account of the longer winter; on the highlands it lasts longer than on the coast for the same reason.

Clinical Signs.—In some the disease appears to come in attacks; in others this intermittency is not so evident. In one patient under my care just at present attacks come on about four times a day in the cold weather, each one lasting about fifteen minutes. The attack commences with pallor and tingling; this passes on to cyanosis and a dull ache; finally flushing and a burning sensation are noted. This last stage is often accompanied by swelling, due to ædema.

When the attacks are persistent for some time, the patient may have brittle nails, chronic onychia, shrinking of the finger pulp, and occasionally dry gangrene at the finger tips.

Pathology.—Lewis's view is that the real cause of the malady is a local defect in the vessel whereby cold acts unduly upon the vessel walls. It is only because the temperature effect upon these vessel walls is reinforced from time to time by increase of nervous tone that the idea that the malady is primarily a vasomotor one has arisen. Lewis states that the main vessels affected are the arterioles of the parts involved, and that the primary cause of the disease is in those vessels and not in the nervous system. In many of these patients there is scarcely an "attack", these small vessels being always in spasm, though from time to time a little extra "pinch" occurs, when the phenomenon becomes manifest (or more manifest) clinically.

Adson (Rochester) maintains that Raynaud's disease results from hyperactivity of the vaso-

constrictor reflexes and that the fault therefore lies in the central nervous system. He points out that in his cases, after complete removal of the vaso-constrictors supplying the lower limb, it was impossible to evoke vasomotor spasm, however intense the stimulus. The occasional persistence of spasm in the upper extremities was attributed to failure to remove all fibres. The more favourable results from the radical procedure recently introduced for the upper extremities support this inference. Adson has shown a patient, operated on five years ago, who is free from symptoms.

Lewis and Kerr return to the attack.

The mechanism of an attack appears to be a closure at relatively low temperatures, of relatively large vessels; this closure is believed not to be reflex in nature, there being no evidence that vasomotor impulses confine themselves to the tip of the digit. Moreover, vasomotor reflexes created by cold are known to be conveyed very widely and not to limit themselves to the small skin territory to which cold has been applied.

Lewis and Kerr are thus led to the conclusion that in patients with Raynaud's disease there is an abnormality of the arteries displaying itself in hypersensitivity to relatively low temperatures, and that the effects of cold are not produced through the intervention of the nervous system. On the basis of physiological experiment they believe that the vaso-constrictor nerves pass to the vessels of the limb in the mixed nerve and not along the arterial coats. They do not suggest that because a vaso-motor impulse does not determine the abnormal condition of spasm it contributes nothing to the tone of the vessel.

Villaret, Justin-Besançon and Cachera, writing in *The Lancet* of September 1, 1934, postulate subsidiary vasomotor centres throughout the body; they think that localized vasomotor spasm might help in explaining temporary hemiparesis, aphasia, scotoma of migraine, erythromelalgia, Raynaud's disease and some manifestations of Ménière's vertigo.

The intense constrictor response in the smaller arteries causes the pallor. What of the cyanosis? It is not so easy to explain. Possibly the following is an explanation. Subsequent to the intense constriction, a certain amount of relaxation ensues, but owing to the anemia and the fall of skin temperature the amount of H-substance released is so great as to cause capillary dilatation; and though the rate of flow is reduced because of the degree of vaso-constriction which still persists, the capillary and anastomotic fields gradually fill. The gaseous exchange goes on; therefore the semistagnant capillary stream continues to give off its oxygen and to take up carbon dioxide.

Adson's views of the factors responsible for the various reactions are somewhat as follows. An undue degree of vaso-spasm may be attributed to an exaggerated stimulus transmitted by the vaso-constrictor fibres of the sympathetic system.

Lewis and Kerr's views, as expressed in The British Medical Journal of January 11, 1930, are

that the fault lies in the vessel walls, so that a stimulus of normal strength may induce a reaction out of all proportion to the impulse which instituted it.

Possibly the ultimate solution will be found in a combination of circumstances—an abnormal degree of tone in the smaller arteries and an unduly sensitive condition of the skin.

In a recent article Lewis (T) postulates "nocifensor" nerves as nerves capable of effecting changes in the skin locally and without reference to the central nervous system, and as nerves liberating potent substances from cellular elements of the skin into surrounding spaces, and thus controlling partly or wholly within the skin important elements of defence (including inflammation).

Differential Diagnosis.—In the differential diagnosis the following conditions have to be eliminated: (a) Cervical rib; (b) arthritis, with vascular changes of the Raynaud type; (c) arteriosclerosis; (d) Buerger's disease.

There are certain tests which temporarily relax spasm; this procedure is often adopted before proceeding to treatment." (i) The extremities may be immersed for thirty-five minutes in water at 130° F. (ii) Hyperpyrexia may be produced by intravenous injection of typhoid vaccine. (iii) Spinal anæsthesia may be induced. (iv) The peripheral nerve may be anæsthetized. All these are an attempt to cut out the vaso-constrictor element and to secure a maximum of vaso-dilatation. A positive result has a treble significance. (a) It affords proof of the existence and degree of the spasmodic element. (b) It excludes or assesses the existence of any degree of permanent occlusion change (but I would remark here that the reactive hyperæmia test is a better indication of that). (c) It offers valuable information on the prospects of success in treatment

It is unfortunately true that where Raynaud's disease is concerned no constrictor eliminating procedure secures complete relaxation, and we are forewarned therefore that treatment on those lines is apt to prove disappointing.

Treatment.-In the treatment of Raynaud's disease the patient should be protected from the cold with gloves and long-sleeved undervests; he should avoid living in a place with a long winter. Massage, exercises and diathermy do not seem to give much benefit. With vaso-dilators, such as acetyl-choline, the results seem to vary. I have given considerable relief by this method in some cases, injecting acetyl-choline every other day for many weeks. On the other hand, it is said by some observers to be decomposed immediately it enters the tissues and to become inert. Of course it is unsafe to ascribe improvement to one measure when several are being used, but in some cases in which relief followed the use of acetylcholine it was practically the only measure employed. "Lacarnol" (muscle extract) and "Padutin" (a pancreatic extract) have been used by some observers with success, so they claim.

Alternate methods of suction and pressure, as described by Landis and Gibbons, might prove helpful. Of this method I have no personal experience, nor can I find much about it in the literature.

Sympathectomy, particularly the radical operation of ganglionectomy, is often satisfactory; the results may be dramatic for a time, but later may be disappointing. The attacks become less frequent and less severe; pain becomes less and superficial gangrene may be prevented. In the neck, Royle and Coates(8) approach the ganglion from the front; it is not devoid of risk, owing to the subclavian vessels. Adson approaches the ganglion from behind. Flint(9) has had much success in giving relief with sympathectomy, especially in the lower limbs. Heale, (10) of Melbourne, advocates cervicodorsal sympathectomy, even though recurrence has taken place in a certain number of cases. Trumble, (11) of Melbourne, in doing lumbar sympathectomy, resects a portion of the sympathetic trunk at about the level of the third lumbar vertebra; in this way preganglionic fibres are destroyed, whereas in the upper limb the postganglionic fibres and their cell-stations are destroyed. Trumble thinks this is probably the reason why the results in the lower limbs have been better. Royle and Hoets, of Sydney, have had brilliant instances of temporary relief, but recurrence has usually taken place.

In one case of Raynaud's disease in which I did lumbar sympathectomy the patient got complete relief for one year, but the symptoms then recurred.

Coates, of Melbourne, has had success in several mild cases of Raynaud's disease with periarterial sympathectomy. He also approves of this operation for early diabetic gangrene, for chronic ulcer of the leg and as a preliminary to a skin grafting of the foot or leg. He states that constriction of the artery at the time of stripping, followed (in a few minutes to one hour) by a flushing of the limb beyond the seat of stripping, is beyond question. Shaw, of Melbourne, has done this operation in injuries to the limbs and amputation stumps, in which the vascular conditions were not unlike those of Raynand's disease; the patients have done very well after it.

In one case of Raynaud's disease in which I did this operation on the brachial artery, flushing of the hand came quite quickly and there was some improvement in the Raynaud's condition, but this subsequently relapsed.

Thrombo-Angiitis Obliterans (Buerger's Disease).

The disease known as thrombo-angiitis obliterans or Buerger's disease is an example of the inflammatory type. It has intervals of improvement which are probably coincident with the opening up of pathways of collateral circulation; but as these become affected the symptoms occur with increased intensity until additional channels become available. The additional channels in other turn become affected and so the process continues, until the

blood flow is so completely arrested that death of the tissues ensues; the veins are affected later and to a lesser degree.

Mtiology.-It has not yet been definitely established whether the disease is due to an infection or to an endocrine, metabolic or constitutional disturbance. There is one very constant feature. namely, heavy cigarette smoking. The incidence of the disease in the Jewish race has been somewhat overstated. None of my patients that I can recall were Hebrews. W. J. Mayo suggests that methynol, in a vaporous form from the burning paper of cigarettes (like the methynol in wood alcohol in "bootleg" liquor), may be one of the causes of the ill-effects. The disease generally occurs in males round about forty years. There are occasionally septic foci, such as infected teeth and tonsils. There is proof of the inflammatory nature of the underlying pathological process in the arteries and veins; this is also well illustrated in the striking picture of superficial migrating phlebitis which is characteristic of 30% to 40% of cases in the practice of other observers. I cannot say that this is so in my experience.

The last case of thrombo-phlebitis migrans that I saw was in a man over sixty with auricular fibrillation and no sign of thrombo-angitits obliterans. We found strepto-cocci in the gastric contents; from these a vaccine was made. From then on the patient had no recurrence of his trouble; prior to that it had been very persistent. No definite alteration in the blood constituents had been found.

The predominance in the male has led some observers to suspect the prostate, but without much evidence. The disease may occur in the labouring man as in the man with a sedentary occupation. One patient of Coates first noticed his trouble on an expedition to the South Pole. The family incidence has been striking in the experience of some observers.

Pathology.—There are two essential elements in the pathology of the disease, an acute inflammatory process involving arteries, veins and sometimes nerves, and a thrombotic occlusion of those vessels. The lumen of the vessels is filled with an adherent clot; in the advanced stages the clot will be practically homogeneous with the vessel wall. Gross canalization may be apparent.

Microscopically, one notices in the arteries a pathological process similar to that in the veins, that is to say, the wall is the site of an intense inflammatory reaction with leucocytes and a few lymphocytes; in addition some giant cells are present either in the wall or in the thrombus. Organization of the clot by ingrown fibroblasts is the final stage in the pathological process. There may be attempts at canalization. The principal effect of the inflammatory changes in the arteries is slow occlusion of the affected vessels.

In Buerger's disease occlusion and collateral circulation struggle for supremacy; if the intervals between relapses are short and the time for adequate collateral circulation is brief, trophic changes and gangrene are likely to ensue. Conversely, if the intervals are long, collateral circulation becomes adequate and sufficient supply of blood to the distal areas is assured.

Complications.—Coronary artery disease occasionally coexists with Buerger's disease. Because of this, Samuels takes an electrocardiogram before undertaking intravenous therapy. Occasionally intraabdominal and cerebral thrombosis occurs.

Symptoms.—The following sequence is the rule: Onset, with weakness, numbness or fatigue in the extremities, followed by pain on walking, then the pain on rest (the pain is worse at night with the limb under the bed-clothes; to some extent it is relieved by hanging the leg over the side of the bed), and finally the agonizing pain of ulceration and gangrene. There is a subjective coldness of the extremities. A cessation of perspiration in the affected foot occurs. The pain after walking is generally known as claudication; in its typical form it is a comparatively late symptom and almost pathognomonic of arterial obstruction. Practically all these symptoms may apply either to arteriosclerosis or thrombo-angiitis obliterans.

Signs.—There may be some muscular atrophy of the affected extremity, particularly in the advanced stages. Bony atrophy is often visible in the radiographs in long-standing cases. Trophic disturbances of the skin and nails are present in the later stages. A pink condition (or rubor) of the feet is often present; this is a pink cyanotic tint of the toes and the soles of the feet, which gives way to intense pallor when the limb is elevated. The colour is alow in returning when the limb is replaced in the horizontal position.

Differential Diagnosis.—In the differential diagnosis of this disease it is important to remember: (a) Its occurrence in young males, (b) its association with excessive cigarette smoking, (c) the occasional history of thrombo-phlebitis migrans.

The disease is to be distinguished from the following conditions:

1. Arteriosclerosis. This may occur in either sex. It is a disease of older people, though occasionally it occurs in people as young as forty years of age. It is often associated with diabetes mellitus. In diabetics, arteriosclerosis appears at an earlier age and calcification of the peripheral arteries is much more intense than in ordinary arteriosclerosis. Calcification would negative Buerger's disease. The symptoms and signs are much the same in arteriosclerosis as in thrombo-angiitis obliterans, namely, pain, coldness, intermittent claudication, ischemia, rubor, deficient arterial pulsation and gangrene; the reactive hyperæmia time is considerably increased in both. Thrombo-phlebitis migrans is not seen in arteriosclerosis. Syphilitic arteritis resembles arteriosclerosis clinically.

2. Raynaud's disease. Raynaud's disease generally occurs in females. It is usually symmetrical, the symptoms are confined to cold weather and pain is

not so severe and not continuous. Colour changes in Raynaud's disease generally go from dead white to deep cyanosis to bright pink. In advanced cases superficial gangrenous ulcerations may be present. Scleroderma is quite often associated with long-standing cases of Raynaud's disease, In Raynaud's disease ischæmia cannot be elicited by elevation of the limbs, as in the occlusive arterial diseases.

3. Acrocyanosis. Acrocyanosis is a vaso-spastic disease. Its symptoms occur only in cold weather and more often in females than males.

4. Frost-bite. Frost-bite (of which trench-feet is a severe example) occurs only after exposure to cold.

5. Erythromelalgia. Erythromelalgia is extremely rare and, in the opinion of Lewis, comprises several affections. It is characterized by agonized burning sensations in the extremities when they are maintained in the dependent position.

6. Polycythæmia vera (Osler's disease). Polycythæmia vera is often associated with localized gangrene of the toes or fingers. It is identified by the characteristic appearance of the patient, particularly the congested and brick-red colour of the skin. Enlargement of the spleen and the polycythæmic blood count are also diagnostic.

7. Embolism. Embolism of the larger arteries of the extremities may sometimes offer difficulty. There is usually a preexisting cardiac history. It is characterized by a sudden onset of severe pain, with an almost immediate feeling of coldness and numbness in the entire limb. Occasionally this happens after lobar pneumonia.

Malaria and typhus fever. Malaria and typhus fever may occasionally be complicated by gangrene of the extremities.

Cervical ribs. Cervical ribs frequently cause symptoms and signs simulating arterial disease.

10. Fallen arches. The pain of fallen arches is frequently felt, not only in the foot, but in the limb above; naturally it is worse after exercise, so might simulate claudication.

11. Sciatica. The pain of sciatica is sometimes associated with coldness and numbness of the lower part of the limb, which may suggest an obstructive arterial lesion; it also is worse after muscular exercise.

Treatment.—As the exact cause is unknown, there is no specific remedy. Our main aim is to encourage a collateral circulation that will compensate for the occlusion of the existing vessels. If the collateral circulation is insufficient to maintain the life of the distal parts, gangrene ensues.

I think it must be admitted that in Australia—in Sydney, at any rate—we have not concentrated sufficiently on patient measures to encourage this collateral circulation and thus to save the limb; too often we have been led aside by so-called curative measures, and when they fail, have adopted amputation rather precipitately. We are encouraged to do this because of the intense pain from which the

patient is often suffering, pain that is frequently not relieved very much by the ordinary doses of morphine. In fact, because of this comparative lack of response to morphine, these patients are sometimes thought to be malingerers.

Samuels, of New York, makes a strong plea for extreme conservatism. He claims to have treated over 300 patients in the last eight years, and in only one had he performed amputation. He attained these results by concentration on the following measures: (a) Rest in bed, with the leg in the horizontal position; (b) absolute prohibition of smoking; (c) intravenous injection of 300 cubic centimetres of hypertonic saline solution (2%, 3% or 5%) every other day; (d) local treatment of the ulceration.

Of course one looks for a septic focus in the teeth, tonsils et cetera.

If we sufficiently realize the tendency towards the formation of extensive collateral circulation, even in the severest cases of gangrene, we shall bide our time and wait for a line of demarcation to form, which is always followed by spontaneous exclusion of dead tissue and healing of the residual ulcer.

Of course we have learned that successful therapy in almost any disease today is dependent upon early diagnosis. If the disease is recognized before the development of gangrene, much can be accomplished towards improving collateral circulation and preventing later serious consequences. The stimulation of collateral circulation is of greater importance than the relief of symptoms. The patient naturally will require all our reassurance on this point.

Although keeping the limb horizontal may temporarily increase the patient's pain, it is essential to adopt that procedure when gangrene is impending. In the milder cases rest need not be

Smoking must be absolutely prohibited; its place may be taken by "Minties".

Heat is valuable, but it must be used with care. In the cases without ulceration or gangrene a comfortably hot Sitz bath for ten minutes a day is valuable. The bath is filled with hot water to the level of the hips. It is also wise to wrap the entire limb up to the groin in cotton wool. Diathermy is a valuable agent for the safe production of heat; the hyperæmia is of distinct benefit both for the relief of symptoms and for the enhancement of collateral circulation; it should not be used in the presence of ulceration or gangrene. Preferably each foot is placed on a metal electrode; each of these electrodes is connected to a pole of the apparatus. Baking is not desirable.

Postural exercises are a valuable adjunct. They were introduced by Buerger. They are of most benefit in the early stages, before ulceration or gangrene has appeared. They proceed somewhat on these lines. The limb is elevated to an angle of 45° for two minutes. It is left in a dependent position for three minutes and in a horizontal

position for two minutes. This should be repeated four or five times and should be done three or four times in the day. Follow with a hot Sitz bath. Continue exercises and baths for a long time after all symptoms have disappeared.

Intermittent negative pressure, although favoured by some, is not recommended by Samuels as an aid to increasing the peripheral circulation because of the risk of dissociating a clot.

Intravenous saline therapy. Samuels has had excellent results with the use of intravenous injections of 2% and 3% sodium chloride. Meyer used Ringer's solution subcutaneously with good results. Samuels thinks that the repeated stretching effect on the smaller vessels is responsible for the improvement in arterial circulation. The warm feeling in the limb may not appear for a few weeks, but is usually permanent thereafter. Coates (Melbourne) doubts the value of the method.

Samuels gives the following directions regarding the technique. (I have never seen it tried to the extent that Samuels recommends, so cannot speak authoritatively of its value.) It is advisable to use doubly distilled water in the preparation of the solutions. To prepare the 5% solution, 15 grammes of chemically pure sodium chloride are dissolved in 350 cubic centimetres of distilled water. For the 3% solution, 9 grammes of sodium chloride; for the 2%, 6 grammes are used. (The additional 50 cubic centimetres of distilled water are necessary to allow for evaporation during sterilization.) The solution is filtered through filter paper into a 500 cubic centimetre "Pyrex" flask and boiled over a gas burner for ten minutes. The solution is resterilized after at least eight hours for another ten-minute period. After cooling it is ready. It is poured into a "Salvarsan" burette of 300 cubic centimetres capacity and warmed to body temperature. Transparent gum rubber tubing allows one to see whether there is a back-flow of blood into the tubing. A rustless steel needle, 19 gauge, one and a half inches long, is used and is inserted into the cephalic or basilic vein. If the patient should show a tendency to local thrombosis, the strength should be reduced to 3% or 2%. If there is trouble with the arm veins, the external jugular vein may be tried. The head is turned to one side and the patient is instructed to distend his cheeks with air, slowly, with his mouth partly open; the needle is directed from above downwards. About ten minutes are taken for the injection. An injection is given three times a week for three months, and then gradually the frequency is decreased until nine months of treatment have been given; but if the patient is not relieved after the first three months, the tri-weekly injections are continued. When ulceration or gangrene is present the saline injections are given thrice weekly until healing has occurred and are then continued for a few months

Non-specific protein therapy. Intravenous injection of triple typhoid vaccine does not appear to

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offer any advantages over other methods of treatment and is not free of risk in thrombo-angiitis obliterans.

Intermittent pressure on veins. Collens and Wilensky⁽¹²⁾ claim to have completely or partially relieved pain and to have healed ulcers by inflating a cuff on the thigh to sixty to eighty millimetres of mercury for alternating periods of two minutes, the treatment lasting up to twelve hours a day.

Operations on the sympathetic nervous system. It must be emphasized that it is only in the early stages of thrombo-anglitis obliterans that vasomotor disturbances are common; simple measures will accomplish what ganglionectomy can effect.

Trumble, Heale and Coates, of Melbourne, and Royle and Hoets, of Sydney, recommend lumbar sympathectomy in early cases, but it is doubtful if we in Australia have paid sufficient attention to the more simple measures of promoting collateral circulation. I have seen several cases in which sympathectomy has failed, and I think even its advocates realize that it is only in the early stages of the disease that it is of any value.

Acetyl-choline. I have tried acetyl-choline, but without giving any relief. One uses it on the assumption that it is an efficient peripheral vaso-dilator, so that it is somewhat of a shock to read that Carmichael and Fraser hold that this drug is decomposed as soon as it enters the tissues and that intravenously its effects last only a few seconds.

Tissue extracts. The use of de-insulinized pancreatic extract has been suggested, one to five cubic centimetres being given intramuscularly or subcutaneously. It appears to be effective in relief of the pain of intermittent claudication. I am unable to ascertain from the Sydney drug firms that we have any such products here.

Treatment of gangrene and ulceration. Trauma may play a very important part in the causation of gangrene. Operative procedures are sometimes carried out on the toes on the assumption that the pain in the toe is due to an ingrowing toe-nail; such a procedure may precipitate local gangrene. Absolute rest in the horizontal position is indicated; smoking must be absolutely prohibited. It is wiser to drop the old distinction between "dry" and "wet" gangrene. It is better to consider all forms of gangrene as consisting of dying or dead tissue, separated by a demarcating area of infected tissue from living healthy tissue. The infection may be macroscopic, with actual pus formation, or it may be microscopic with a minimum of purulence, so-called "dry" gangrene.

Such efficient antiseptics as Dakin's solution, "Calsol", "Tolamine", cannot be improved upon, but it must be remembered that they must be used in the strength in which they are made up, not watered down, as is so often done. Frequent wet dressings of these solutions on gauze are used, or the foot is immersed in a copious warm bath of them three times or more a day for ten to thirty minutes. Following the foot-bath, a good anæsthetic

ointment is liberally applied to the ulcerated part. During the acute or spreading stage of gangrene, the patient undergoes the most excruciating pain; there is a temptation to resort to amputation, but the painful stage of gangrene is not of long duration—it lasts a few weeks at the most. Throughout all stages of gangrene it is necessary to guard against a temptation to meddle; do not cut away toes, tendons, bones et oetera. Surgical amputation of the toes is unnecessary and dangerous.

The chances of recovery from gangrenous lesions in the upper extremities are excellent, because of the presence of a much better natural blood supply in these limbs. However, recently I myself amputated several fingers because of the excruciating agony in a patient who was very difficult to handle. A few days after operation most of his pain had gone.

Complications. Coronary artery disease occasionally coexists; because of this, Samuels takes an electrocardiogram before undertaking intravenous therapy. Agius (Malta) mentions a case in which frequent anginal attacks of the coronary thrombosis type were associated with very typical signs and symptoms of Buerger's disease; the onset of the former preceded that of the latter by several years. Occasionally intraabdominal thrombosis or cerebral thrombosis occurs.

Amputations. If it is necessary to perform amputation, it is useful to learn from the experience of Rochampton Orthopædic Hospital which kind of amputation allows the best artificial limb. I give some extracts from R. Money's article in the medical students' journal of July, 1933:

The Chopart mid-tarsal amputation, when fitted with a special boot, has been found very satisfactory and is advocated in preference to a Syme where feasible (only the os calcis and astragalus are saved).

Below the Knee.—The ideal below-knee amputation was found to be one with six to seven and a half inches of tibia, about one inch less of fibula and with a posterior transverse scare.

Through the Knee,—Stephen Smith amputation through the knee-joint was found to be unsatisfactory.

Above the Knee.—All amputations of the Carden, Gritti-Stokes variety are definitely contraindicated.

The ideal femur stump should measure twelve inches and no more from the great trochanter.

Arteriosclerosis.

Arteriosclerosis usually occurs after middle-age. Heredity plays a part in its causation. It is more common in the male, but is frequent in females. It is probably due to a disturbance of metabolism.

Pathology.—The "intimal" type of arteriosclerosis is the most important and the most common. This is the type that is responsible for the symptoms of deficient circulation in the extremities. There is no inflammatory reaction in the arterial walls as is seen in thrombo-angiitis; the process is a degenerative one. The symptoms in the extremities are caused by the obstruction to arterial onflow, and the obstruction is produced either by the thickening

of the intima or by a thrombus that forms on an ulcerated plaque. Diabetics are more prone to show calcification of the arteries. The veins are not involved in arteriosclerosis; this is one of the distinguishing features.

Symptoms.—Symptoms do not differ from those encountered in other organic obliterative diseases, such as thrombo-angiitis obliterans. Patients have paræsthesias of the toes and feet, coldness of the extremities, pain and intermittent claudication.

Treatment.—The primary purpose is the attempt to improve the collateral circulation in the extremities, this is more difficult than in thromboangiitis owing to the greater age of the patient. Rest is essential and moderation in smoking should be

The application of heat is useful. The safest way is to wrap the extremities completely in a warm covering, such as lamb's wool. A hot Sitz bath is given once or twice a day for ten minutes, sitting. Diathermy should be used daily or every second day for twenty minutes; it should be given at the degree of intensity best tolerated by the patient. Baking is not recommended.

Postural exercises are useful; except with coexisting coronary disease. Hypertonic saline solution, 2%, is sometimes given intravenously in small doses (occasionally with success), but not in the presence of coronary disease. Typhoid vaccine is contraindicated. Vaso-dilators are useless. Operations, such as ganglionectomy and periarterial sympathectomy, are of no avail.

Preparations of de-insulinized pancreatic extract are said to be a useful adjunct for those patients suffering from pains in the legs after walking; one cubic centimetre to five cubic centimetre doses are given intramuscularly every second day.

Local care of the feet is essential, especially in diabetics. Diabetes, if present, should be treated with insulin and diet. In non-diabetics a salt-free diet does not seem to be of much importance.

In gangrene, if amputation is necessary, the best spot is the lower third of the thigh; no drains should be used. Nitrous oxide anæsthesia or "Sodium Evipan" injected intravenously is suitable.

SUMMARY.

- 1. An attempt is made to classify peripheral vascular disease into capillary and arterial sections.
- 2. These again are subdivded into the varieties of each.
- 3. Various tests for the assistance of diagnosis are enumerated, but special stress is laid upon the "reactive hyperæmia" test as modified by Pickering.
- 4. In Raynaud's disease emphasis is laid upon Lewis's views about the presence of slight structural changes in the vessel walls. Mention is also made of the immediate relief that may follow in Raynaud's disease by means of operations upon the sympathetic system, but that this is apt to be only temporary.

- 5. Amongst the occlusive arterial diseases a good deal of space is devoted to the conservative methods of treatment in Buerger's disease in order to avoid
- 6. Cold is seen to be one of the most important factors in the ætiology of many vascular diseases.

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CEREBRAL SOFTENING.

By J. B. CLELAND, M.D., Marks Professor of Pathology, University of Adelaide; Honorary Pathologist, Adelaide Hospital.

In 3,000 post mortem examinations at the Adelaide Hospital carried out between 1920 and 1935 there were 94 examples of cerebral softening due, or probably due, to atheroma and thrombosis in cerebral vessels, and 27 attributed to other causes, making a total of 121.

Of the 94 cases, there were 63 in which atheroma of the cerebral vessels was specially noted; of these, 39 were in males aged 45, 49, seven patients were in the fifties, 14 in the sixties, 12 in the seventies, three in the eighties; the age of one was unrecorded. Twenty-four were in females whose ages were 45, 48, 49, two patients were in the fifties, seven in the sixties, seven in the seventies and five in the eighties.

In 31 atheroma was not apecially noted, but was probably responsible for most of these cases. Of these, 18 were in males whose ages were 44 (? tumour), two patients were in the fifties, ten in the sixties, two in the seventies and three in the eighties. Thirteen were in females whose ages were 27, 30, 47, five patients were in the fifties, three in the sixties and two in the seventies.

In the 94 cases the ages were 27, 30, eight persons were in the forties, 16 were in the fifties, 34 in the

¹A summary prepared for a demonstration and discussion on a case of cerebral softening at the Adelaide Hospital on August 3, 1936.

sixties, 23 in the seventies, eleven in the eighties, and in one instance the age was not recorded.

The 27 cases of cerebral softening due to causes other than atheroma and thrombosis were classifiable under the following figures.

Malignant endocarditis and embolism (males aged 33, 45, 46 and 51, females aged 13 and age not recorded)

Infective cerebral softening from septic abortion (a woman aged 46)

Associated with coronary infarction or fibrosis of cardiac muscle, probably due to embolism from cardiac thrombi [males aged 26 (fibrosis of cardiac muscle), 85 and 76, and a woman aged 56]

Hypertrophied and dillated hearts, probably from

Hypertrophied and dilated hearts, probably from hyperpiesis, presumably attributable to dislodgment of cardiac thrombi (a male aged 46 and a woman aged 49)

Mitral stenosis, probably from dislodgment of cardiac thrombi (a male aged 47 and females aged 28, 30, 48 and 50—also with cardiac infarction)

Softening following tying of the carotid artery, epithelioma of palate (a male aged 60)

Embolus (?) from vegetations on the aorta (a male aged 64)

Embolus (?) dislodged from atheromatous ulcer or plaque in the aorta (males aged 60, 70, 79) Melanoma of the eye, secondary deposits, cerebral softening, but no obvious deposit (a woman

aged 41)
Degenerated areas on the surface of the brain attributed to old trauma (males aged 32 and 75, and a woman aged 37)

Reports of Cases.

A CASE OF NORMAL PREGNANCY EXHIBITING POSITIVE ASCHHEIM-ZONDEK REACTION WITH URINE DILUTED ONE IN FIFTY.

> By THOMAS H. SMALL, Woollahra.

Mrs. I.L., aged twenty years, consulted me on August 31, 1936. The last menstruction had occurred on June 16, 1936. Pelvic examination revealed a uterine pregnancy of approximately two months.

She had a severe homorrhage without pain on September 7 and another on September 21. On the last occasion the fundus was at the level of about three and a half to four months. This may have been due to a loaded bowel. I was doubtful and decided to have an Aschheim-Zondek test done to exclude hydatidiform mole. This was carried out at the Royal Hospital for Women at Paddington, with urine diluted one in twenty, using three mice. The result was positive. A further test was then done with urine diluted one in fifty, using three mice. The result was again positive. I was away at this time, and asked Dr. Ida B. Saunders to see the patient and advised termination of the pregnancy. The people were unwilling to have this done and were advised by Dr. Saunders to wait, as she had doubts as to the correctness of this diagnosis, on clinical grounds, and also because she knew of a case in which a colleague at the Royal Hospital for Women had emptied a uterule of a normal three menths'

pregnancy when a positive Aschheim-Zondek reaction with diluted urine had indicated a hydatidiform mole. It is not known how many mice were used or what dilution of prine.

By the time I had returned the patient had felt movements. The pregnancy continued in a normal manner and the patient was confined of a living female infant on March 24, 1937.

There was no engorgement of the infant's breasts, such as occurs sometimes, and is said to be due to excessive formation of anterior-pultuitary-like substances.

I think it is better to report this case rather than to hush it up, because too much reliance apparently can be placed on this test, and others should know of this possible pitfall in diagnosis. On the face of it, a positive Aschheim-Zondek reaction with urine diluted even one in fifty is not of itself a positive sign of hydatidiform mole, although a dilution of one in ten is sometimes regarded as sufficient.

Reviews.

PHYSIOLOGY.

BAINBRINGE AND MESSIES'S well-known "Essentials of Physiology" has now reached its eighth edition. This, like the two previous editions, has been edited and revised by Professor H. Hartridge.

Several new chapters have been written by the editor in his latest revision, but the book retains its usual form. The original purpose of the book, which was written "primarily with the object of meeting the requirements of the medical student preparing for a pass examination in the subject of physiology", has been kept in view. Within the limits so frankly stated this text book will continue to be a great help to the student, owing to the conciseness with which the subject is presented.

With such a presentation it cannot be expected that all sections will be dealt with equally satisfactorily. Some of the biochemical material needs further revision, as it does not accord with present knowledge, or is expressed in a way likely to mislead the junior student. For example, the impression is given that only some half dozen amino-acids are necessary for life and that the rest function mainly as fuels and can be dispensed with. The specific dynamic action of protein is given as 10% instead of the usually accepted figure of 30%. A number of other minor errors occur in the biochemical portions. The hydrocarbon carotene (spelled "carotin") is described as a phenanthrene derivative, and the tryptophane derivatives indole and skatole are spoken of as purines.

It is evident that the rapid progress which is occurring in biological chemistry is making satisfactory treatment of biochemical material increasingly difficult in elementary text-books of physiology. A solution of the difficulty is complicated by the fact that biochemical processes are every day being shown to play a more important part in physiological phenomena.

The sections on the special senses and on certain aspects of the circulatory and respiratory mechanisms have been very satisfactorily treated, as might be expected from the editor's attainments in these branches of physiology. A fuller description of the electrocardiogram would have been desirable, and the kinetic energy of the blood, which represents such an important fraction of the work of the heart at high outputs, should not have been ignored.

A very useful feature of the book is the unusually full index with which it is provided.

¹ "Bainbridge and Mensies' Essentials of Physiology", edited and revised by H. Hartridge, M.A., M.D., Sc.D., M.R.C.P., F.R.S.; Eighth Edition: 1826. London Longmans, Green and Company. Mediam svo, pp. 696, with illustrations. Price: 148. net.

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The Medical Journal of Australia

SATURDAY, JUNE 26, 1937.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: Initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

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WORK ON NUTRITION IN AUSTRALIA.

The third report of the Commonwealth Advisory Council on Nutrition is to hand, and we have also received the first annual report of the Queensland Nutrition Council. The Commonwealth Council and the Queensland body are really part of the same organization, for according to the Queensland report the preliminary meeting that resulted in the formation of the Queensland Nutrition Council was called inter alia "to give effect to the desire of the Commonwealth Advisory Council that a Local Committee should be formed in this State". At the same time, if newspaper publicity and propaganda on food in relation to health are any indication of real activity and desire for achievement, Queensland is much more alive than any of the other States.

The most important item in the Commonwealth Advisory Council report is an account of a survey of the children of the north-eastern portion of South Australia, that has been made by Dr. F. W. Clements. In another place in this issue a special abstract of Clements's work is published. The Council expressed its appreciation of the work of Dr. Clements, and decided to send a copy of his report to the Government of South Australia. It

also approved a proposal that the survey should be continued into the north-western portion of New South Wales and the south-western portion of Queensland. It is hoped that at a later date surveys of the north-western portion of Victoria and the interior of Western Australia will be undertaken. Readers of this journal will remember that the Commonweaith Advisory Council determined to undertake a family survey, in order to discover the type and quantity of food consumed by the people. Apparently in New South Wales, Victoria, Queensland and South Australia this is being done. No mention of either Tasmania or Western Australia is made in this regard. In New South Wales 406 booklets have been issued; in other words, 406 family diets are being investigated. This is not a very large number when the population of the State is considered, and when we remember that every stratum of society needs to be investigated. Admittedly those families with incomes at or below the basic wage level are more likely to have an ill-balanced diet, but it must never be forgotten that even a moderately good income does not mean that a sufficient quantity of the right kind of food is consumed. No figures are given for the number of families being investigated in Victoria-"steady progress is being achieved". In Queensland 100 families and in South Australia 148 families are being investigated. Some time ago the Commonwealth Council appointed a biological chemist and a statistician, in the persons of Dr. Geoffrey Bourne and Dr. W. A. Carr Fraser, to make analyses and to convert the analyses into standardized units. Both these officers have made reports to the council; their reports are mostly concerned with recommendations for future action. Professor Harvey Sutton has also submitted to the council a report on the possibility of obtaining accurate information on the extent of under-nourishment among school children. On his recommendation the council has adopted a resolution advising the appointment for six months of a medical officer who would, under Professor Sutton's direction and with the assured cooperation of the medical officers of the Education Department, examine the possibilities of obtaining this information. Certain recommendations were

made by the Council on popular education and propaganda, recommendations that are already being carried out effectively in Queensland. Two final resolutions were also adopted. One was the expression of a pious hope about the daily supply of milk for school children; the other recommended to the National Health and Medical Research Council the formulation of standards, especially of weight, for white bread, wholemeal bread and the several varieties of wheaten bread commercially classed as fancy bread.

The report of the Queensland Nutrition Council is an interesting document. The members of this committee are certainly active; no one could justly accuse them of half-hearted effort. The chairman of the council is Professor H. K. Lee, Professor of Physiology in the University of Queensland; and it is of great satisfaction that members of the Queensland Branch of the British Medical Association are taking a prominent part in the doings of this body. The report is divided into several parts. The first sets out the history of the Council, and the second deals with its activities as a local committee of the Commonwealth Advisory Council on Nutrition. There are also sections on publicity, education, research and "ways and means". We do not propose to discuss this report at any great length, but would merely point out that a useful and determined effort is being made to lead the people of Queensland along the paths of dietetic rectitude. In this matter the Council enjoys the whole-hearted cooperation of the Queensland Press. Attention was drawn some months ago to. a "Nutrition Supplement" that was published in the Brisbane Courier-Mail, and a second supplement will shortly make its appearance. Talks over the air have been given for many months and have been carried out according to a wellarranged roster; and articles have been published at regular intervals in country newspapers on the principles of diet and on cooking and nutrition. Perhaps one of the factors that has brought success to the efforts of the Queensland council is that its workers are all voluntary workers.

It is not to be expected that everyone will agree with all the efforts of either the Commonwealth

or the Queensland organization; differences of opinion will be mainly on matters of minor importance. It is, however, necessary that the medical profession and the public should be thoroughly aware of the efforts that are being made for the common weal, and of the enormous amount of ground that still requires to be covered.

Current Comment.

DIRECT VENOUS PRESSURE ESTIMATIONS IN AMBULATORY CARDIAC PATIENTS.

THE detection of the earliest objective signs of heart failure is a constant object of search on the part of the cardiologist. Subjective symptoms in their earlier phases are notoriously unreliable. Thus a multiplication of functional tests for cardiac efficiency as measured by effort response, vital capacity estimations, and determination of cardiac output include periodical determinations of venous pressure. It is the value of this particular information that has been the subject of investigation in ambulatory cardiac patients by Dr. A. R. Berger, of New York.1 He has reasoned that the initial load in the ventricle just prior to systole is the pressure of the blood within it; this in turn is determined by filling from the auricle, which is modified by venous pressure and venous return. For him who subscribes to the backward failure hypothesis of cardiac decompensation, the measurement of venous pressure on theoretical grounds should be the best objective evidence of early failure. The venous pressure in the pulmonary circuit can-not, of course, be determined in man, but the pressure in the right auricle is readily measurable by the original method or by a modification of the method of Moritz and yon Tabora. The apparatus consists of a manometer capable of being adjusted so that its zero reading is in the same horizontal plane as the right auricle. The system contains a sterile 5% sodium citrate solution, and the needle, which is of the standard size, is inserted into the medial basilic vein. Readings are begun after fifteen minutes of recumbency. All readings are checked and the Valsalva experiment is performed each time. The results embodied in this paper are obtained from an extensive study, extending over four years, of 68 male patients in the adult cardiac clinic of the Belle View Hospital. They included a rheumatic group, a group designated "arteriosclerosis and unknown", and a series of hypertensive patients with sundry others. The control group consisted of 20 male patients convalescing from minor illnesses and of a parallel age group. These 20 normal individuals showed an average venous pressure of 7.7 centimetres of water, with a range of 2.9 centimetres between minimum and maximum.

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¹ The American Heart Journal, April, 1937.

The 68 patients suffering from well-advanced heart disease, but not from congestive failure, had an average venous pressure of 7.6 centimetres, but with a gradual fluctuation between maximum and minimum. The highest reading was recorded in the "rheumatic-hypertension-arteriosclerosis group". Berger has illustrated his article with some useful graphs containing simultaneous readings of vital capacity, weight, edema and venous pressure over a series of ten to twelve determinations. He noted also the distinct correlation between the consistently rising venous pressure and the appearance of cardiac failure as has been described by Eyster. However, the usual clinical signs were apparent just as soon as the elevation of venous pressure. The highest venous pressure obtained in the normal group did not exceed 10.4 centimetres, which agrees with previously published figures. There is thus considerable normal variation, which must decrease the value of the test in the abnormal state. It further appears that venous pressure can become elevated above normal without other signs of cardiac failure being present and without seeming to presage a threatened cardiac decompensation. The exact nature of this mechanism is not clear. Variations in intramuscular tone of skeletal muscle influences the venous return to the heart, or it is possible that. venous spasm may occur, a kind of essential venous hypertension. There is no doubt that marked local venous spasm can occur when a vein is injured, for example, by venipuncture.

Berger concludes that venous pressure itself cannot be used to prognose the onset of congestive failure. The sign of a raised venous pressure is therefore not a most reliable or necessarily an early sign of failure. Lewis has insisted for many years upon the importance of clinical observations of venous pressure; even rough bedside tests of the observations of the degree of venous distension have been accorded considerable significance. There is no question but that such observations are of confirmatory value and of considerable aid in estimating the daily progress in one direction or the other of congestive heart failure; but it seems, from the present study, that a rise of venous pressure may occasionally occur in quite normal subjects, and that as an early sign of impending cardiac breakdown it must be considered as no better than the objective information referred to at the commencement of this comment.

THE BACTERIAL FLORA OF THE MOUTH AND THE STOMACH.

It is always assumed that there must be a direct relationship between the bacterial flora of the mouth and that of the stomach. Most authorities recognize that the occurrence of acute gastric erosions may be associated with frank oral sepsis, while it is always advised that the hygiene of the mouth is a necessary adjunct to the treatment of digestive disease and an essential part of the preoperative preparation for operations on the stomach. Evidence of direct infec-

tion of the gastric mucosa from acutely or chronically inflamed nasal accessory sinuses has been brought forward by some workers, and another interesting link is now provided between the bacterial flora of the stomach and that of the mouth by Marion Hood and Lloyd Arnold.1 These workers did not use for their observations patients suffering from gastro-intestinal disease nor those with primary anæmia. They made cultures from material aspirated from the stomach and took special care to adjust the hydrogen ion concentration within the usual limits of bacterial growth. These were compared with cultures made by inoculating on to plates swabs which had been rubbed across the back of the tongue. Preliminary tests were made to ascertain whether the bacterial content of the mouth varied at all in different parts of the mouth, and these showed that the back of the tongue not only yielded evidence of the heaviest degree of infection, but also yielded the most diverse flora. Staphylococci were the organisms most commonly found both from tongue and stomach, and next to these streptococci. When the mouth was inoculated with the readily recognized Bacillus prodigiosus the same organism was recovered also from the stomach, and it was found to disappear from the mouth in an average time of two and a half hours and from the stomach in a little over one hour. The effect of washing out the mouth was next investigated. Other workers have found that the use of an antiseptic, such as a weak solution of hexyl resorcinol (1 in 4,000), accelerated the rate of disappearance of bacteria from the mouth, but Hood and Arnold did not find that this antiseptic was superior to normal saline solution. They concluded that the mechanical effect of washing out the mouth was more important than the deterrent action of a disinfectant. This conclusion accords well with the general beliefs concerning the values of various dentifrices and mouth washes. Experiments to discover the relationship between the swallowing of saliva and the inoculation of the stomach with bacteria did not give any striking results. Even when the flow of saliva into the mouth was diverted, as by the use of a sucker, neither the hydrogen ion concentration of the stomach contents nor its bacterial flora was materially altered. This work establishes that there is a striking resemblance between the amount and kind of the bacterial flora of the mouth and the stomach. When it is realized that infection with the Vincent's spirillum, for example, occurs in the lung, and that its source is almost certainly the mouth, the importance of oral sepsis as the seeding ground of more or less distant organs cannot be gainsaid. As to any possible effect of saliva on the stomach contents, these experiments are too brief and restricted in scope to yield much information. But if any confirmation is indeed needed for what seems a self-evident proposition, that a clean stomach is unlikely to be found without a clean mouth, it is certainly found here.

¹The American Journal of Digestive Disease and Nutrition, March, 1987.

Special Abstract.

A NUTRITIONAL ASPECT OF SOUTH AUSTRALIA.

Ar the first meeting of the Advisory Council on Nutrition appointed by the Federal Government it was decided that an inquiry should be conducted into the physical condition of children living in remote areas of inland Australia. The results of the first survey, made by F. W. Clements in the arid regions of northern South Australia during the beginning of the present year, are presented in the third report of the Advisory Council. An abstract of the findings is published below.

All children of school age up to fourteen years were surveyed and the parents of those too young to attend school were asked to bring them also for examination. There was an excellent response to this request. The report embodies the painstaking physical, clinical and radiographic investigations which then followed, the findings being classified as "satisfactory", "unsatisfactory" or "doubtful".

The school pupils each wrote out a list of the foods eaten on the day previous to examination, the presumption being that if, on a day chosen at random, a given child had swallowed a representative collection of protective articles, its usual diet might be taken to be satisfactory. The positive value of these lists was great, but on the negative side was of less worth, though the details supplied to the investigators not seldom revealed a high consumption of fermentable carbohydrates, such as sweets, biscuits and cakes, and an absence of protective food factors.

A descriptive note is necessary of the terrain embraced in the survey. By all ordinary standards it is barely habitable. In shape, the region resembles the letter "L", inclined slightly backwards. The roughly horizontal limb inclined slightly backwards. The roughly horizontal limb stretches from the town of Peterborough in a north-easterly direction to Cockburn, on the border of New South Wales. The nearly vertical limb, running northward from Peterborough, comprises an area in which are the mid-north towns of Orroroo, Carrieton and Hawker. Still further north, in a hot, barren and rainless land, live the people of Blinman and Marree. In and about the region described there are scattered homesteads, station holdings and dusty farms. Both segments of the "L" are pierced by railways which come to an apex at Peterborough. From Marree in the north the line sweeps west and north to Ocdnadatta and on to Alice Springs in Central Australia. recent times the Peterborough-Cockburn railway was the trade route to Broken Hill, and the people of the towns upon it are railway workers and th They enjoy the concession of free transport of supplies by train and so pay at a reduced rate for food and household goods. They are an inbred race, the men so conservative and narrow in outlook that they frequently refuse to leave their dull settlements even on a promise of promotion; gat the women, good housewives are rare. in this Peterborough sector is poor, but vegetables grow if given water; but water costs one shilling for each hundred gallons. This is supplied from a railway service and is supplemented by drinking water collected in tanks. There are no dairymen, but privately owned cows were found in twenty-six out of seventy families. Two families in this area relied on goats for their milk supplies. this section of country Clements examined 212 children in a total child population of 217. Carlous, stopped or missing teeth were found in 116, or 64-5% of this number; 18 children were suffering from rickets; the nurser; 18 children were suffering from rickets; the nurritional state of a further 47 was unsatisfactory. Enlarged and infected tonsils were present in 31 subjects (14%) and were in nine cases the cause of unsatisfactory nutrition. In the 212 children the state of health and nutrition was satisfactory in 140.

In the farming communities of the mid-north there are scattered flocks and some dairy herds, and efforts are made to grow wheat. Most of the farmers produce scanty

supplies of vegetables and own cows, but hard times and drought have lowered the general standards of living, many of the people subsisting on rations. Clements's survey here disclosed, among 225 children examined, 188 whose standard of nutrition was good and 16 in which it was prov. Of these latter, four had rickets and were members of rationed families. In nine the tonsils were enlarged and infected. The dental survey showed that in many places in the farming belt the children's teeth were in an excellent state and free of carles and fillings, while elsewhere in this country dental defects were rife. Here was a community whose members lived all under practically identical conditions, in which at least some wheat, mutton, milk and vegetables were to be had, but in which the conditions of the children's teeth varied from good to very bad. The explanation of the observed facts is that in this area of the survey there are two distinct mineral belts, with corresponding differences in the surface soil. The area forms a part of the Adelaide series, of which a geological survey has been made by Professor W. Howchen. The rock formation consists of a series of dipping strats, the two most important being a calcareous belt tending north-north-east across the area, and to the west and east of it a series made up of quartites, achists and slates with a low lime content. The influence of these geological factors is clearly revealed by the results of the dental examination. In the schools situated on the shale belts the incidence of affected mouths ranged from 58% to 65%; dental deficiencies of some kind were found in 37% of scholars from schools on the limestone. In all, 101 children (48%) had missing, stopped or decayed teeth. The group of 225 produced 42 children with enlarged, infected tonsils and adenoids. A state of generally poor nutrition was present in 16, or 7% of the total.

A tri-weekly train brings perishable foods to the towns of the mid-north, at a cost 50% above the ruling prices in Adelaide. In this sector, 242 children were presented for examination. The group contained 195 whose physique was satisfactory, 22 in which it was held to be doubtful, and 25 in which it was unsatisfactory. In nine of these latter evidence of rickets was detected. Dental defects were found in 136 examinees, or 56% of the total, and throat infections in 65.

In the far north the Commonwealth railway line runs from the town of Hawker to Marree, and the population of railway workers, station hands and teamsters lives at sidings along the track. Some foods are carried free of freight charges from Quorn. Fruits and vegetables are as much as 150% dearer than in Adelaide. There are few kitchen gardens, since water, at a price of one shilling per 100 gallons, is scanty. In this sector 164 children (98% of the entire child population) were surveyed. Nutrition was unsatisfactory in 47 cases (28%), tonsillar and adenoid infection existed in 14, 30 children were affected by rickets, and 54 (33%) had affected or absent teeth. In this remote district the standard of living was below that in any other sector. Fifty-two families possessed only six cows between them, and only eleven households were certain of a daily supply of milk. The situation regarding cream, eggs and fruit was little better.

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Among the sheep stations along the Peterborough-Cockburn line, and on that from Hawker to Marree, 69 children were seen; an additional 72 lived so far away as to be out of reach of the survey. On these holdings cows were found, and well-stocked vegetable gardens. These satisfactory living conditions were reflected in Clements's findings. Of these 69 children, only three fell below the accepted standards, and in each of these a septic focus in the throat was found. No child showed signs of rickets; but in 32 (46%) some of the teeth were carious, stopped or nosent.

Massing the figures resulting from the surveys made in all sectors, we find that throat infections were the causal factor in a small number of instances of the children's ill-health. In 47 cases the cause could not be accurately defined. Rickets was responsible for 61 cases. The disease, as here noted, was of the borderline or pre-borderline type. One, and perhaps the only, advantage of life in these regions is that ample sunlight tends to combat the rhachitic effects of a poor dietary, and often

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prevents the development of rickets as an obvious clinical entity. It may be taken, therefore, that Clements regards the evidences of rickets found by himself as circumstantial rather than direct. The most evident signs were found in infants aged between twelve and twenty-four months. The mothers of these children stated that they were restiess at night, when they sweated about the head, and that they had lost both weight and appetite. There were frequent histories of repeated colds and of catarrhal affections of the respiratory tract. The heads of these infants were relatively too large as compared with their bodies, and the skin and mucous membranes were distinctly pale. Very often they were children of a fat and flabby type. The muscles and ligaments were in a state of hypotonia, and in many cases the frontal bones showed bossing. A Harrison's sulcus was commonly evident on the chest. rather than direct. The most evident signs were found the chest.

To procure confirmatory evidence skiagrams were taken of the epiphyses of the wrist in the case of children aged five months and two and a half years respectively. These films showed that the last half centimetre of the diaphysis was blurred and the epiphyseal line ragged and frayed in appearance. In the presence of such findings in infants it was noted that the general condition of the older children in a given family was unsatisfactory; they were restless, pailed, under normal weight and size, bad-tempered, lacking in appetite and suffering from muscular hypotonia. Deformities, such as recession of the sternum and Harrison's sulci, were to be found. Skiagrams of the wrists of these older children showed the epiphyseal line to be wavy and irregular in outline, while coarsening of the trabeculations suggested that at the growing ends there were disturbances in the activities of normal bone construction. It is perhaps true that these appearances cannot be taken as due to rickets with complete certainty, but the very aspect of the children, together with the history of ailments affecting their younger brothers and sisters, more than justifies such a suspicion. The presence of rickets was therefore not diagnosed in children above the age of eight years, partly because no X ray films showing unmistakably rhachitic appearances were obtained. The cause of a generally lowered nutritional state was in these instances therefore classified as undetermined. But these children as a class were underweight, pale, without subcutaneous fat and plainly showing evidence of hypotonia. Here the wrist skiagrams showed the presence of irregularity in the epiphyseal lines, with coarse trabeculation, hardly evidence enough to warrant an unequivocal diagnosis of borderline rickets, but sufficient, when considered in conjunction with a diagnosis of mild rickets in younger members of the same family, to justify the assumption that these eight-year-old children were suffering from the past or present effects of an inadequate diet. Clements past or present effects of an inadequate diet. Clements believes that had his radiographic investigations been confined to children of school age, the presence of rickets might easily have been overlooked. It is therefore pertinent to ask why, if the disease was so mild as to be diagnosable only with difficulty, it should be a cause for any concern. The answer is that hand in hand with retarded physical development resulting from bad nutrition goes a very obvious backwardness at school.

Here, then, amongst 925 children, were 61 affected by Here, then, amongst 925 children, were 61 affected by rickets of borderline type, a total of about 6%. This was the finding in a country with more than 300 days of sunshine in each year. The explanation is that these 61 cases occurred in 31 families, the heads of which were railway employees or men working at haphazard intervals upon farms or stations. In the households of the railway workers the wages, though regularly paid, were dissipated in drink and on inefficient housekeeping, and in the families in which rickets occurred the dwellings were almost always untidy. The rural labourers, frequently unemployed through climatic conditions and economic depression, were the victims of their environment, forced with their families to subsist upon rations consistently low in fat-soluble vitamins. There is no doubt, besiden, that the poor nutrition of some children examined had its origins not in rickets, but in a diet of high carbohydrate content and of low fat value.

The barren and arid nature of much of the country visited during the progress of the survey suggested that cases of scurvy might be discovered, yet none were found. But the population as a whole consumed large quantities of potatoes, some children eating them three times daily. This fact probably explains the complete absence of

scorbutic disease.

Nor was there evidence of disorder due to deficiency of vitamins A and B. A mild hyperkeratosis of the skin of the arms was occasionally seen, but without any history of night-blindness, so that the condition could not be attributed to lack of vitamin A.

Many children needed surgical removal of enlarged and infected tonsils and adenoids. There were no less than 159 such children in the total of 925 examined. The septic foci present in such cases seemed not to result in mal-nutrition, which appeared to require an unsuitable diet or some other unfavourable factor to ensure its appearance.

Scattered cases of trachoma, to the number of 39, were encountered along the Peterborough-Cockburn railway line, and others in the far north, but no relationship between trachoma and malnourishment was established during the survey, which was carried out during the summer months, a period of increased incidence of this disease.

In only two children were abnormal pulmonary signs detected, and this despite the fact that the sandstorms of the region are a possible source of chronic pulmonary

Careful examinations were made for evidences of cardiac disease. None were found, nor was any history elicited of growing pains, growing pains, rheumatic fever or chorea. The two medical practitioners in the area surveyed stated that they The two had seen no case of rheumatic fever in the north or north-east of South Australia. Congenital heart disease was discovered in three instances, and four children had functional heart murmurs.

In spite of the relatively small area of the northern part of South Australia which came within the scope of the survey, the area covered included the majority people living north of 32° S. Vast spaces in the northern part of South Australia are uninhabitable, especially in its western portions, and in the north-east, a land of droughts, the stations, which are few in number, are closed

for years in succession.

The Advisory Council on Nutrition has conveyed to Dr. Clements its great appreciation of the quality of the work done and of the excellent report which he has submitted. It has recommended that a copy of the report should be sent to the South Australian Government. The proposal that the survey should be continued into the north-western portion of New South Wales and the south-western portion of Queensland was approved by the council. This tour will commence as soon as the seasonal conditions permit of continuous motor travel.

British Wedical Association Mews.

SCIENTIFIC.

MEETING of the New South Wales Branch of the British Medical Association was held on April 29, 1937, in the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, On. LINDSAY A. DET, the President, in the chair.

Spastic Paralysis.

Dr. R. A. Green read a paper entitled "Spastic Paralysis"

Ds. N. D. Royle read a paper ent'tled "The Surgical Treatment of Spastic Paralysis (see page 979).

Dr. Royle illustrated his remark, by the exhibition of moving pictures of experiments carried out on goats. Pictures were shown of a goat with the sympathetic nerve supply removed from the left hind limb. There was an on in posture when the left limb was compared with the intact limbs.

A picture of a decerebrate animal was shown; the sympathetic nerves had been removed from the left hind limb 130 days prior to decerebration. This showed an alteration in posture and in the myotatic reflex. The denervated limb exhibited the phasic and not the posture part of the reflex.

A picture of goats under the influence of adrenaline and ephedrine was shown. In the goat under the influence of adrenaline the left hind limb was shown with the loss of posture, while all the rest of the limbs appeared in extension.

The fourth was a striking picture exhibiting the development of tone under the influence of ephedrine. The fore-limbs were shown gradually extending. It was striking to observe that under the influence of ephedrine the goat assumed the posture of a decerebrate animal. Dr. Royle explained that these changes were due to the alteration in spinal blood supply and that the failure of the left hind limb to extend in the adrenaline experiments illustrated that adrenaline had little effect after sympathectomy.

The fifth film consisted of pictures of experiments on the spinal animal under the influence of ephedrine. A resistance to passive movement was shown in the moving pictures, whereas in the spinal animal there should have been complete flaccidity.

The sixth picture illustrated the effects of superior thoracic ganglionectomy in diminishing tone on the contralateral side.

The seventh set of pictures showed the effects of superior thoracic ganglionectomy in a patient suffering from spastic quadriplegia. In the picture taken before the operation the child was shown walking with a spastic gait, which was not seen in the pictures of the patient taken some years after the operation.

DR. EDGAR M. STEPHEN expressed his appreciation of Dr. Green's paper. He was glad that Dr. Green had laid stress on the fact that injury was not the main cause of spastic paralysis. He spoke of the excellent work that was being carried out at Canonbury, the convalescent home for children supported by the Australian Jockey Club. It was very pleasing to see a child of as young as three years of age learning by conscious effort to use muscles once paralysed. He thought that there was no need to be too hopeless in discussing the condition of a child with the parents when it was first seen, for a great deal could be accomplished if constant and unremitting care was used. It was his experience that many of these children were ansemic and that improvement in the mental condition began to occur once the ansemia was corrected. He had noted, moreover, that the child's mentality improved to a remarkable degree when once it began consciously to use

DR. W. T. D. Maxwell said that although he was a general and not an orthopsedic surgeon, he was keenly interested in the subject under discussion. He paid a tribute to the work of Dr. Royle and said that he had followed the history of the work and knew that in certain conditions dealt with by the general surgeon, good results were obtainable by sympathetic nerve surgery. He referred particularly to thrombo-angitis obliterans (Buerger's disease), to Raynaud's disease, and to senile gangrene caused by atheroma. Periarterial sympathectomy in the last-named condition was a dangerous procedure. Dr. Maxwell said that he had been asked to operate on a man who was suffering from gangrene of the toes of one foot; the toes of the other foot were blue. He had noted after amputation of the affected limb that the other limb became suffused and warm and the toes red and rosy—a phenomenon observed also by Leriche, and made possible in the presence of atheroma by the fact that only the larger arteries were sclerosed. This would appear to confirm the supposition that the sympathetic nerve supply was bound up with a spinal reflex, the mechanism of which, however, remained obscure. In conclusion, Dr. Maxwell referred to the excellent practical indication afforded by the change in the opposite limb, for by the performance of a lumbar ganglionectomy the temporary result gained by what amounted to a physiological peri-

arterial sympathectomy in the second limb was made permanent.

Dn. R. Anger. Money said that he had enjoyed both papers, and made a plea for earlier diagnosis. He said that if nothing was done until the child was three or four years old and the spastic paralysis had become firmly established, it was really too late to undertake treatment. When a condition likely to lead to spastic paralysis was suspected, the new-born child should be subjected to lumbar puncture or to cisterna magna puncture, and if clear fluid was obtained, then subarachnoid hæmorrhage could be excluded. In comatose children or in the presence of convulsions a needle might be inserted at the sides of the anterior fontanelle; if only a little clear fluid was obtained, the presence of a subdural hæmatoma might be excluded. The needle might then be pushed further under the arachnoid into the cerebrum itself. If no conclusions were reached, it might then be necessary to do a full encephalography. If the results of all these examinations failed to reveal any abnormality, it was then possible to say that the condition was one of cerebral agenesia. Dr. Money thought that if the procedure he had outlined was adopted in all doubtful cases before the spastic condition was established, it might be possible to prevent its onset and to do something for a small percentage of the patients.

Dr. Lorimer Doos agreed with Dr. Money about the importance of diagnosis, but stressed the fact that blood in small quantities was found so frequently in the cerebrospinal fluid of the new-born infant, particularly the premature infant, as to be almost physiological. He felt that there was a tendency to dismiss the average spastic infant with some brief directions about home care, and possibly some arrangements about routine physical therapy. There was also a tendency to regard many of these infants as grossly mentally defective and incapable of any response to treatment and education. Admittedly, in a certain number of these infants little or no improvement could be expected; but Dr. Dods thought that the majority might be benefited by appropriate treatment. To be able to offer appropriate treatment an extensive knowledge of special fields of medicine, surgery and social science was required, and Dr. Dods felt that this treatment would best be provided by a team composed of physician, neuro-surgeon, psychiatrist, orthopædist and physical therapeutist, in association with physical therapy, speech defect, almoner and occupational therapy clinics.

DR. GILBERT PRILLIPS said that he had been impressed with the lantern slide shown by Dr. Royle, demonstrating the increased vascularity on one side of the spinal cord which followed the removal of its sympathetic nerve supply. He thought, however, that there was at least one very formidable piece of evidence against the hypothesis that central changes in blood supply could be responsible for modifying postural reflex action. He pointed out that if the discharge from a single anterior horn cell to a skeletal muscle was recorded galvanometrically in a decerebrate animal during a constant stretch of the muscle tendon of from ten to twenty grammes, it was found that the nerve cell fired off, as the result of proprioceptive stimulation, at a rate of from nine to eleven times per second; this discharge continued at that rate so long as the stretch remained constant. If the stretch was increased the rate of firing was increased; if the stretch was removed the cell ceased to discharge. This mechanism was beautifully graded and extremely flexible. If under such conditions of constant stretch the abdominal sympathetic chain was stimulated on either side, at any level, with shocks calculated to be adequate for the autonomic nerve fibres, there was found to be absolutely no alteration in the rate of firing of the anterior horn cells. Dr. Phillips here referred to a paper of his which had been published in the Journal of Physiology, Volume LXXV, containing the proceedings of the Physiological Society for May 14, 1932. He said, moreover, that if the whole of the abdominal sympathetic chains were extirpated on both sides there was no alteration, either at that time or subsequently, in the rate of single cell discharge in response to constant proprioceptive stimulation.

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Dr. Phillips went on to say that for still another reason he found it difficult to believe that changes in cerebral blood supply, resulting from removal of the inferior cervical and upper thoracic sympathetic ganglia, could be considered to be the cause of any alterations which might occur in the postural activities of the contralateral limbs. It had been shown that the sympathetic nervous system was the site of persistent vaso-constrictor impulses (he referred to a paper by Adrian, Bronk and Phillips, published in Volume LXXIV, Number 2, of the Journal of Physiology for 1932). These disappeared when the pre-ganglionic connexions were cut; and it could be inferred from this that removal of the pre-ganglionic sympathetic supply to the post-ganglionic cells in the superior cervical ganglion, by the operation suggested by Dr. Royle, might produce considerable changes in the cerebral vascular pattern. This would be so because the operation would terminate the normal persistent post-ganglionic vaso-constrictor impulses to the cerebral blood vessels.

Dr. Phillips further pointed out that it had been noted in the last few months by a number of observers, working in different laboratories, that within ten days to two weeks after pre-ganglionic denervation of post-ganglionic cells, the latter began to discharge spontaneously, probably as the latter began to discharge spontaneously, probably as the result of their sensitization to sympathomimetic sub-stances in the blood stream. He thought that it was unlikely, therefore, in the light of the spontaneous return of vaso-constrictor impulses, that much, if any, alteration in the cerebral blood supply would result from extirpation of the superior thoracic and inferior cervical sympathetic ganglia, unless the post-ganglionic cells in the superior cervical ganglion were also removed.

Dr. Green, in reply, said that he wished to thank Dr. Money for what he had said about early diagnosis. It was a fact, however, that lumbar puncture was not of great value by itself, and many of these infants were so shocked value by itself, and many of these infants were so shocked that they would not stand any further interference. He agreed with what Dr. Dods had said, and thought it was important that all these children should be carefully followed up. It should be feasible for any such cases occurring in the obstetric hospitals to be referred to a clinic at which their development could be watched.

Dr. Royle, in reply, said that the results of operation on the sympathetic nervous system showed the view advanced by Dr. Phillips to be incorrect.

NOMINATIONS AND ELECTIONS.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Cumpston, Howard Bruce, M.B., B.S., 1936 (Univ. Sydney), Western Suburbs Hospital, Croydon.
Gill, Robert Chalmers, M.B., B.S., 1937 (Univ. Sydney), Sydney Hospital, Sydney.

The undermentioned have applied for election as members of the Tasmanian Branch of the British Medical Association:

Redmond, Kenneth Bodell, M.B., B.S., 1936 (Univ. Sydney), General Hospital, Hobart.
Chalmers, John Sneddon, B.Sc., 1931, M.B., B.S., 1936 (Univ. Sydney) General Hospital, Hobart.

Correspondence.

A SYMPOSIUM ON CANCER.

Sn: Mr. Poate's thoughtful and interesting letter on the treatment of cancer by radiation methods calls for comment in one or two places.

- The Medical Research Council's report referred to does state that radical surgical removal is performed at the Marie Curie Hospital in cases of operable breast cancer, and also in cancer of the body of the uterus. All cases of carcinoma of the cervix without distant metastases are treated by radium—the Stockholm technique. This number now runs into over a hundred cases a year (110 in 1929 and 136 in 1930, the five-year survival rates for those years being 34.5% and 42.6%).
- 2. Carcinomata of the breast are in a somewhat different category. I think that most will agree with Mr. Poate that in an operable case radical surgery with pre-operative X radiation is the best treatment available at present.

With regard to treatment of the breast by radium, I think that one of the weak points of most methods has been in relying upon interstitial application alone. I can remember seeing a case treated by Mr. Keynes where recurrent nodules were present in nearly every needle scar. Surface application removed these and might have prevented them.

At the Middlesex Hospital the method was to insert needles, deep to the tumour if possible, and then to give heavy irradiation from the surface. At the time of which I speak this was given by a radium mould, but later the "gramme unit" or radium bomb was used. Needless to say, X radiation could have been employed.

I note that of the cases of primary (not recurrent) breast cancer so treated at this hospital in 1931, fourteen are living and thirty-five are dead, which gives a survival rate of just over 28%. These cases were practically all inoperable. I speak from knowledge, as I was working in the department at the time, and the breast cases that came to us were the rejects from the surgical wards. Without being startling, that is a fair salvage.

Hutchison's survey, as far as radium is concerned, deals largely with Keynes's own cases, and as his method was popular at the time, in all probability the majority of cases were treated this way. I consider the absence of super-ficial treatment in some form a definite defect in technique.

However, as previously stated, in operable cases I think surgery the safest procedure.

3. Epithelioma of the lip. For nearly two years at the Middlesex Hospital, and subsequently since my return to Australia in 1933, I have practised the treatment of this condition by means of radium applied on a surface mould. This avoids the possibility of cellulitis and lessens scarring. It is more comfortable to the patient, and applies the greatest intensity where it is most needed. I have not yet failed to make the primary growth disappear, whether on skin or mucous surface. Admittedly, dissection of the glands is frequently needed. The disadvantages of this method are that it calls for greater skill and more this method are that it calls for greater skill and more radium. It is effective in primary cases, and also where a recurrence has developed after surgical removal, and can be used for either upper or lower lip. Should I develop an epithelioma of the lip, I would be content to have it treated by a radium mould. In fact, the more I see of radium the more I feel that it is best applied from a surface, whether external or intra-cavitary

At certain hospitals in London nearly all buccal and pharyngeal growths are now treated by means of the radium "bomb" or mass unit. This in most cases does away with the necessity of interstitial radium. The one gramme unit at the Middlesex Hospital is so busy with such cases that it cannot be spared for other regions of the

A recent development is the manufacture of artificially radio-active substances and the invention of the cyclotron. It is interesting to speculate whether these new and more powerful radiations may not alter the whole field of radiotherapy.

Yours, etc., John Mayo. 170, North Terrace, Adelaide, June 7, 1937.

Voi

Books Received.

BUCHANAN'S MANUAL OF ANATOMY, INCLUDING EMERYOLOGY, edited by J. E. Fraser, D.Sc., F.R.C.S.; Sixth Edition; 1937. London: Ballilere, Tindail and Cox. Double crown 9me, pp. 1783, with filustrations. Price: 35s.

SURFACE ANATOMY, by W. R. Roberts, M.R.C.S., L.R.C.P., with a foreword by A. N. Burkitt, M.B., B.Sc.; 1937. Australia: Angus and Robertson Limited. Medium 8vo, pp. 104, with illustrations. Price: 7a. 6d. net.

PHYSIOLOGY AND PATHOLOGY OF THE HEART AND BLOOD-VESSELS, by J. Pleach, M.D. (Budepest), M.D. (Germeny), L.R.C.P. and S. (Edinburgh and Glasgow); 1987. Oxford: University Press; London: Humphrey Milford. Demy 8vo, pp. 200, with illustrations. Price: 22s. 6d. net.

Diary for the Wonth.

JULY 21 JULY 22

JULY 28 JULY 29

Queensland Branch, B.M.A.; Branch.
New South Wales Branch, B.M.A.; Organization and Science Committee.
New South Wales Branch, B.M.A.; Council.
(Quarterly).
Western Australian Branch, B.M.A.; Council.
Victorian Branch, B.M.A.; Branch.
South Australian Branch, B.M.A.; Council.
Queensland Branch, B.M.A.; Council.
New Bouth Wales Branch, B.M.A.; Executive and Finance Committee.
New South Wales Branch, B.M.A.; Branch.
New South Wales Branch, B.M.A.; Clinical meeting.
Queensland Branch, B.M.A.; Council.
New South Wales Branch, B.M.A.; Council.
South Australian Branch, B.M.A.; Branch.
New South Wales Branch, B.M.A.; Council.
South Australian Branch, B.M.A.; Council.
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New South Wales Branch, B.M.A.; Branch.
New South Wales Branch, B.M.A.; Council.
South Australian Branch, B.M.A.; Council.
South Australian Branch, B.M.A.; Council.
South Australian Branch, B.M.A.; Council.

Medical Appointments.

Dr. L. E. Clay has been appointed Certifying Medical Practitioner at Avoca, Victoria, pursuant to the provisions of the Workers' Compensation Acts.

Dr. M. C. Gardner has been appointed, in accordance with the provisions of the Workers' Compensation Acts, Certifying Medical Practitioner and Medical Referee at Melbourne, Victoria.

Gedical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum tenentes sought, etc., see "Advertiser", pages xvili to xx.

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DEPARTMENT OF PUBLIC HEALTH, VICTORIA: District Health

Officer.

FREMANTLE HOSPITAL, FREMANTLE, WESTERS AUSTRALIA: Junior Resident Medical Officer.

MARRICKVILLE DISTRICT HOSPITAL, MARRICKVILLE, NEW SOUTH WALES: Resident Medical Officer.

TARA DISTRICT HOSPITAL, TARA, QUEENSLAND: Medical

THE EASTERN SUBURES HORPITAL, WAVERLEY, NEW SOUTH WALES: HONOTARY Officers.
THE UNIVERSITY OF MELBOURNE, VICTORIA: Senfor Lecturer in Histology and Embryology.

Medical Appointments: Important Potice.

MEDICAL PRACTIFICATES are requested not to apply for any appointment referred to in the following table without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.I.

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New South Walks: Honorary Secretary, 135, Macquarie Street, Sydney.	Australian Natives' Association. Ashfield and District United Friendly Societies' Dispensary. Balmain Unites Friendly Societies' Dispensary. Leichhardt and Petersham United Friendly Societies' Dispensary. Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney. North Sydney Friendly Societies' Dispensary Limited. People's Frudential Assurance Company Limited. Phoenix Mutual Provident Society.
Victorian: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association, Pro- prietary, Limited. Mutual National Provident Club. National Provident Association. Hospital or other appointments outside Victoria.
QUEENSLAND: Honor- ary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17.	Brisbane Associate Friendly Societies' Medical Institute. Proserpine District Hespital. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY Hospital are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.
SOUTH AUSTRALIAN: Secretary, 178, North Terrace, Adelaide.	All Lodge appointments in South Australia. All contract Practice Appointments in South Australia.
WESTER AUSTRALIAN: Honorary Secretary, 205. Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.

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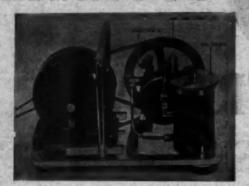
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